

WEBVTT

NOTE duration:"00:59:38"

NOTE recognizability:0.858

NOTE language:en-us

NOTE Confidence: 0.859619759444444

00:00:00.000 --> 00:00:02.170 We have a number of people on

NOTE Confidence: 0.859619759444444

00:00:02.170 --> 00:00:04.080 the zoom already and I'm sure

NOTE Confidence: 0.859619759444444

00:00:04.080 --> 00:00:07.078 there will be more that the join.

NOTE Confidence: 0.859619759444444

00:00:07.078 --> 00:00:12.990 I'm very pleased today to have two speakers.

NOTE Confidence: 0.859619759444444

00:00:12.990 --> 00:00:14.978 Doctors, Hyder and Hanson.

NOTE Confidence: 0.859619759444444

00:00:14.978 --> 00:00:18.540 They will they will go in that

NOTE Confidence: 0.859619759444444

00:00:18.540 --> 00:00:21.886 order and so first is Pharmd Hyder,

NOTE Confidence: 0.859619759444444

00:00:21.890 --> 00:00:24.428 who is a professor of radiology

NOTE Confidence: 0.859619759444444

00:00:24.428 --> 00:00:26.120 and biomedical imaging and

NOTE Confidence: 0.859619759444444

00:00:26.193 --> 00:00:27.869 biomedical engineering.

NOTE Confidence: 0.859619759444444

00:00:27.870 --> 00:00:30.180 He received his PhD in

NOTE Confidence: 0.859619759444444

00:00:30.180 --> 00:00:32.028 biophysical chemistry from Yale,

NOTE Confidence: 0.859619759444444

00:00:32.030 --> 00:00:34.526 where he was also an associate

NOTE Confidence: 0.859619759444444

00:00:34.526 --> 00:00:36.190 research scientist and postdoctoral
NOTE Confidence: 0.859619759444444

00:00:36.257 --> 00:00:38.086 associate with Douglas Rothman.
NOTE Confidence: 0.859619759444444

00:00:38.086 --> 00:00:41.350 He's been in the faculty since 1999,
NOTE Confidence: 0.859619759444444

00:00:41.350 --> 00:00:43.030 seems hard to believe.
NOTE Confidence: 0.859619759444444

00:00:43.030 --> 00:00:46.354 You look very young and currently
NOTE Confidence: 0.859619759444444

00:00:46.354 --> 00:00:48.869 holds dual professor appointments
NOTE Confidence: 0.859619759444444

00:00:48.869 --> 00:00:50.828 in diagnostic radiology
NOTE Confidence: 0.859619759444444

00:00:50.828 --> 00:00:52.787 and biomedical engineering.
NOTE Confidence: 0.859619759444444

00:00:52.790 --> 00:00:55.184 Doctor Hatter is the director of
NOTE Confidence: 0.859619759444444

00:00:55.184 --> 00:00:57.319 the High field horizontal smallbore
NOTE Confidence: 0.859619759444444

00:00:57.319 --> 00:01:00.145 systems at Yale's MRI Research Center.
NOTE Confidence: 0.859619759444444

00:01:00.150 --> 00:01:01.227 He uses MRI.
NOTE Confidence: 0.859619759444444

00:01:01.227 --> 00:01:03.022 He uses magnetic resonance methods
NOTE Confidence: 0.859619759444444

00:01:03.022 --> 00:01:05.227 to map Physiology and chemistry
NOTE Confidence: 0.859619759444444

00:01:05.227 --> 00:01:07.115 that underlie brain function
NOTE Confidence: 0.859619759444444

00:01:07.115 --> 00:01:09.270 for early disease detection,

NOTE Confidence: 0.859619759444444

00:01:09.270 --> 00:01:10.990 but also for targeted drug

NOTE Confidence: 0.859619759444444

00:01:10.990 --> 00:01:12.366 delivery and monetary treatments.

NOTE Confidence: 0.859619759444444

00:01:12.370 --> 00:01:14.974 It's also the founder and director

NOTE Confidence: 0.859619759444444

00:01:14.974 --> 00:01:16.710 of Yale's quantitative neuroscience

NOTE Confidence: 0.859619759444444

00:01:16.776 --> 00:01:19.006 with magnetic resonance course enter

NOTE Confidence: 0.859619759444444

00:01:19.010 --> 00:01:21.060 the only NIH supported programmatic

NOTE Confidence: 0.859619759444444

00:01:21.060 --> 00:01:23.110 effort at Yale on neuroimaging.

NOTE Confidence: 0.859619759444444

00:01:23.110 --> 00:01:24.388 With Mr technologies.

NOTE Confidence: 0.859619759444444

00:01:24.388 --> 00:01:26.944 His work has produced over 100

NOTE Confidence: 0.859619759444444

00:01:26.944 --> 00:01:29.000 peer reviewed publications and

NOTE Confidence: 0.859619759444444

00:01:29.000 --> 00:01:31.580 he's written and edited books

NOTE Confidence: 0.859619759444444

00:01:31.580 --> 00:01:33.740 on functional brain imaging.

NOTE Confidence: 0.859619759444444

00:01:33.740 --> 00:01:36.799 I have to say something that I'm

NOTE Confidence: 0.859619759444444

00:01:36.799 --> 00:01:38.110 becoming increasingly interested

NOTE Confidence: 0.859619759444444

00:01:38.182 --> 00:01:41.060 as I age and he has received early

NOTE Confidence: 0.859619759444444

00:01:41.060 --> 00:01:43.400 career awards from various scientific
NOTE Confidence: 0.859619759444444

00:01:43.474 --> 00:01:45.910 societies and funding scientific
NOTE Confidence: 0.859619759444444

00:01:45.910 --> 00:01:47.708 agencies for me to pleasure.
NOTE Confidence: 0.859619759444444

00:01:47.708 --> 00:01:48.599 To have you.
NOTE Confidence: 0.859619759444444

00:01:48.600 --> 00:01:50.004 Thanks for being here and we
NOTE Confidence: 0.859619759444444

00:01:50.004 --> 00:01:51.170 look forward to hearing from
NOTE Confidence: 0.927893886363636

00:01:51.180 --> 00:01:53.854 you. Thank you, thank you very much
NOTE Confidence: 0.927893886363636

00:01:53.854 --> 00:01:56.020 for that generous introduction.
NOTE Confidence: 0.927893886363636

00:01:56.020 --> 00:01:59.845 I hope I can live up to that introduction.
NOTE Confidence: 0.927893886363636

00:01:59.850 --> 00:02:02.118 It's a pleasure to be here.
NOTE Confidence: 0.927893886363636

00:02:02.120 --> 00:02:05.228 So hopefully you can see the slide.
NOTE Confidence: 0.927893886363636

00:02:05.230 --> 00:02:06.440 Yep, perfect.
NOTE Confidence: 0.88519594

00:02:08.530 --> 00:02:12.200 So my topic today is about dysregulated
NOTE Confidence: 0.88519594

00:02:12.200 --> 00:02:14.420 transmembrane ion gradients.
NOTE Confidence: 0.88519594

00:02:14.420 --> 00:02:17.216 I like cancer invasion of liberation.
NOTE Confidence: 0.88519594

00:02:17.216 --> 00:02:19.776 I believe the latter 4 words are probably

NOTE Confidence: 0.88519594
00:02:19.776 --> 00:02:22.380 more akin to a lot of the audience members,
NOTE Confidence: 0.88519594
00:02:22.380 --> 00:02:24.892 but I'm going to make the connection or
NOTE Confidence: 0.88519594
00:02:24.892 --> 00:02:27.920 try to at least before the the initial
NOTE Confidence: 0.88519594
00:02:27.920 --> 00:02:31.908 part of this title, which is about.
NOTE Confidence: 0.88519594
00:02:31.910 --> 00:02:34.160 So a little bit of.
NOTE Confidence: 0.88519594
00:02:34.160 --> 00:02:36.230 Preface I guess I'm interested
NOTE Confidence: 0.88519594
00:02:36.230 --> 00:02:38.750 in bringing the tablets in why?
NOTE Confidence: 0.88519594
00:02:38.750 --> 00:02:42.350 Because they tell us about the path weights.
NOTE Confidence: 0.88519594
00:02:42.350 --> 00:02:44.744 Which you know end field cells use
NOTE Confidence: 0.88519594
00:02:44.744 --> 00:02:46.830 nutrients to fill their function,
NOTE Confidence: 0.88519594
00:02:46.830 --> 00:02:49.299 but also growth.
NOTE Confidence: 0.88519594
00:02:49.300 --> 00:02:52.150 I'm interested in how cells work.
NOTE Confidence: 0.88519594
00:02:52.150 --> 00:02:53.598 What their made nutrients
NOTE Confidence: 0.88519594
00:02:53.598 --> 00:02:55.046 are in different situations,
NOTE Confidence: 0.88519594
00:02:55.050 --> 00:02:56.602 different states how they
NOTE Confidence: 0.88519594

00:02:56.602 --> 00:02:57.766 get these nutrients.
NOTE Confidence: 0.88519594

00:02:57.770 --> 00:03:00.000 That's actually a very important
NOTE Confidence: 0.88519594

00:03:00.000 --> 00:03:01.860 indicator of disease onset.
NOTE Confidence: 0.88519594

00:03:01.860 --> 00:03:03.740 A lot of fences,
NOTE Confidence: 0.88519594

00:03:03.740 --> 00:03:05.552 but also how they use these
NOTE Confidence: 0.88519594

00:03:05.552 --> 00:03:06.760 nutrients to generate energy,
NOTE Confidence: 0.88519594

00:03:06.760 --> 00:03:08.340 which is crucial for the
NOTE Confidence: 0.88519594

00:03:08.340 --> 00:03:10.512 brain but also to regrow.
NOTE Confidence: 0.88519594

00:03:10.512 --> 00:03:13.670 And disease and damage and so on.
NOTE Confidence: 0.88519594

00:03:13.670 --> 00:03:16.712 And all of these processes happen
NOTE Confidence: 0.88519594

00:03:16.712 --> 00:03:18.165 naturally for normal situations,
NOTE Confidence: 0.88519594

00:03:18.165 --> 00:03:20.055 but they also begin to malfunction.
NOTE Confidence: 0.80978602125

00:03:22.080 --> 00:03:27.376 So these questions that I pose for myself,
NOTE Confidence: 0.80978602125

00:03:27.380 --> 00:03:30.184 as well as my group, my movies and vibrators.
NOTE Confidence: 0.80978602125

00:03:30.184 --> 00:03:32.589 These questions are fundamental for
NOTE Confidence: 0.80978602125

00:03:32.589 --> 00:03:34.919 functional imaging of the brain because

NOTE Confidence: 0.80978602125

00:03:34.919 --> 00:03:37.433 the energy demand for normal brain

NOTE Confidence: 0.80978602125

00:03:37.433 --> 00:03:40.348 work is extremely high and that still

NOTE Confidence: 0.80978602125

00:03:40.348 --> 00:03:43.400 is a very unique property of how.

NOTE Confidence: 0.80978602125

00:03:43.400 --> 00:03:45.507 This organ varies from a lot of

NOTE Confidence: 0.80978602125

00:03:45.507 --> 00:03:47.019 other buildings in the body,

NOTE Confidence: 0.80978602125

00:03:47.020 --> 00:03:49.252 but these questions are also relevant

NOTE Confidence: 0.80978602125

00:03:49.252 --> 00:03:51.085 in cancer and molecular energy

NOTE Confidence: 0.80978602125

00:03:51.085 --> 00:03:53.200 of brain disorders in general,

NOTE Confidence: 0.80978602125

00:03:53.200 --> 00:03:54.580 but especially concert,

NOTE Confidence: 0.80978602125

00:03:54.580 --> 00:03:56.348 because this fundamentally is

NOTE Confidence: 0.80978602125

00:03:56.348 --> 00:03:58.116 a disease of both,

NOTE Confidence: 0.80978602125

00:03:58.120 --> 00:04:01.228 and both requires lots of fuel.

NOTE Confidence: 0.80978602125

00:04:01.230 --> 00:04:03.240 Whenever you need to regulate

NOTE Confidence: 0.80978602125

00:04:03.240 --> 00:04:06.108 to compete for fuel that is a

NOTE Confidence: 0.80978602125

00:04:06.108 --> 00:04:07.940 medical question that it's tough.

NOTE Confidence: 0.80978602125

00:04:07.940 --> 00:04:09.340 So that's my preference,
NOTE Confidence: 0.80978602125

00:04:09.340 --> 00:04:12.268 but my main objective today is to
NOTE Confidence: 0.80978602125

00:04:12.268 --> 00:04:14.692 talk to you about the importance
NOTE Confidence: 0.80978602125

00:04:14.692 --> 00:04:16.040 of transparent votes.
NOTE Confidence: 0.80978602125

00:04:16.040 --> 00:04:18.324 If they're crucially linked
NOTE Confidence: 0.80978602125

00:04:18.324 --> 00:04:20.037 to cellular metabolism,
NOTE Confidence: 0.80978602125

00:04:20.040 --> 00:04:23.210 and this property differs substantially
NOTE Confidence: 0.80978602125

00:04:23.210 --> 00:04:27.010 between normal cells and cancer cells.
NOTE Confidence: 0.80978602125

00:04:27.010 --> 00:04:29.950 Abnormal transmembrane protein and sodium.
NOTE Confidence: 0.80978602125

00:04:29.950 --> 00:04:30.452 Specifically,
NOTE Confidence: 0.80978602125

00:04:30.452 --> 00:04:33.966 I'll talk about protein and sodium gradient.
NOTE Confidence: 0.80978602125

00:04:33.970 --> 00:04:37.260 Are there consequences of health
NOTE Confidence: 0.80978602125

00:04:37.260 --> 00:04:38.576 physiological alterations
NOTE Confidence: 0.80978602125

00:04:38.576 --> 00:04:41.120 occurring with cellular level?
NOTE Confidence: 0.80978602125

00:04:41.120 --> 00:04:43.202 And the two primary things I'll
NOTE Confidence: 0.80978602125

00:04:43.202 --> 00:04:46.060 focus on is the city and salinity

NOTE Confidence: 0.80978602125

00:04:46.060 --> 00:04:47.916 of the interstitial fluid.

NOTE Confidence: 0.80978602125

00:04:47.920 --> 00:04:49.654 These two quantities,

NOTE Confidence: 0.80978602125

00:04:49.654 --> 00:04:53.700 reflected as a proton and sodium ions,

NOTE Confidence: 0.80978602125

00:04:53.700 --> 00:04:54.192 respectively.

NOTE Confidence: 0.80978602125

00:04:54.192 --> 00:04:56.652 They actually regulate central cellular

NOTE Confidence: 0.80978602125

00:04:56.652 --> 00:04:59.790 functions in health as well as improved,

NOTE Confidence: 0.80978602125

00:04:59.790 --> 00:05:01.434 especially cancer under

NOTE Confidence: 0.80978602125

00:05:01.434 --> 00:05:03.452 their bark cancer tomorrow.

NOTE Confidence: 0.80978602125

00:05:03.452 --> 00:05:03.824 Basicness,

NOTE Confidence: 0.80978602125

00:05:03.824 --> 00:05:06.056 which is one of the hallmarks

NOTE Confidence: 0.80978602125

00:05:06.056 --> 00:05:08.259 and even resistance to therapy.

NOTE Confidence: 0.80978602125

00:05:08.260 --> 00:05:10.384 This is actually enhanced

NOTE Confidence: 0.80978602125

00:05:10.384 --> 00:05:11.977 by acidic interstitial.

NOTE Confidence: 0.580223618888889

00:05:14.200 --> 00:05:16.265 Which is actually a consequence

NOTE Confidence: 0.580223618888889

00:05:16.265 --> 00:05:17.917 of popularity by policies.

NOTE Confidence: 0.580223618888889

00:05:17.920 --> 00:05:21.476 I will talk about this in a few minutes.

NOTE Confidence: 0.580223618888889

00:05:21.476 --> 00:05:22.912 But there's also recent

NOTE Confidence: 0.580223618888889

00:05:22.912 --> 00:05:24.259 discoveries from our work,

NOTE Confidence: 0.580223618888889

00:05:24.260 --> 00:05:27.982 and I work with and related groups

NOTE Confidence: 0.580223618888889

00:05:27.982 --> 00:05:31.382 that show that enhance proliferation.

NOTE Confidence: 0.580223618888889

00:05:31.382 --> 00:05:35.029 Which is also a hallmark of cancer

NOTE Confidence: 0.580223618888889

00:05:35.030 --> 00:05:38.510 is impacted by interstitial so,

NOTE Confidence: 0.580223618888889

00:05:38.510 --> 00:05:42.374 so we both these city and the salinity

NOTE Confidence: 0.580223618888889

00:05:42.374 --> 00:05:44.900 of legislation that is crucial.

NOTE Confidence: 0.580223618888889

00:05:44.900 --> 00:05:46.200 A little bit of background,

NOTE Confidence: 0.580223618888889

00:05:46.200 --> 00:05:47.635 I think that's the background

NOTE Confidence: 0.580223618888889

00:05:47.635 --> 00:05:48.496 is probably redundant,

NOTE Confidence: 0.580223618888889

00:05:48.500 --> 00:05:50.817 but for the sake of being bad

NOTE Confidence: 0.580223618888889

00:05:50.820 --> 00:05:52.840 protein and sodium lines are

NOTE Confidence: 0.580223618888889

00:05:52.840 --> 00:05:54.918 vital for numerous processes for

NOTE Confidence: 0.580223618888889

00:05:54.918 --> 00:05:58.340 maintaining blood pressure to fire.

NOTE Confidence: 0.580223618888889

00:05:58.340 --> 00:06:00.188 Only statically we maintain

NOTE Confidence: 0.580223618888889

00:06:00.188 --> 00:06:02.498 a very large sodium gradient.

NOTE Confidence: 0.580223618888889

00:06:02.500 --> 00:06:04.950 Almost two orders of magnitude,

NOTE Confidence: 0.580223618888889

00:06:04.950 --> 00:06:06.220 almost an order of magnitude.

NOTE Confidence: 0.580223618888889

00:06:06.220 --> 00:06:08.752 Sorry. Lending to a very strong

NOTE Confidence: 0.580223618888889

00:06:08.752 --> 00:06:10.018 trance member Radiant.

NOTE Confidence: 0.580223618888889

00:06:10.020 --> 00:06:11.468 Well, certainly, but similarly.

NOTE Confidence: 0.580223618888889

00:06:11.468 --> 00:06:12.916 For for time buildings,

NOTE Confidence: 0.580223618888889

00:06:12.920 --> 00:06:15.000 which is usually measured in terms of pH,

NOTE Confidence: 0.580223618888889

00:06:15.000 --> 00:06:16.460 which if you know it's

NOTE Confidence: 0.580223618888889

00:06:16.460 --> 00:06:17.920 just a log rhythmic scale.

NOTE Confidence: 0.580223618888889

00:06:17.920 --> 00:06:21.728 So even though the pH between interstitial

NOTE Confidence: 0.580223618888889

00:06:21.728 --> 00:06:23.512 and intracellular intracellular

NOTE Confidence: 0.580223618888889

00:06:23.512 --> 00:06:28.744 compartments are 7.4 and 7.2 in PS units,

NOTE Confidence: 0.580223618888889

00:06:28.744 --> 00:06:29.976 it's small.

NOTE Confidence: 0.580223618888889

00:06:29.980 --> 00:06:32.848 But in terms of actual concentration,
NOTE Confidence: 0.580223618888889

00:06:32.850 --> 00:06:35.350 it's again very large.
NOTE Confidence: 0.580223618888889

00:06:35.350 --> 00:06:37.350 There are various mechanisms with
NOTE Confidence: 0.580223618888889

00:06:37.350 --> 00:06:38.886 which are located the cell membrane,
NOTE Confidence: 0.580223618888889

00:06:38.890 --> 00:06:39.910 how regularly.
NOTE Confidence: 0.580223618888889

00:06:39.910 --> 00:06:42.970 A proton and certain levels to
NOTE Confidence: 0.580223618888889

00:06:42.970 --> 00:06:45.488 avoid these mishaps that are
NOTE Confidence: 0.580223618888889

00:06:45.488 --> 00:06:48.660 that sells try very hard before.
NOTE Confidence: 0.580223618888889

00:06:48.660 --> 00:06:49.148 First,
NOTE Confidence: 0.580223618888889

00:06:49.148 --> 00:06:51.100 Megan mechanisms that regulate
NOTE Confidence: 0.580223618888889

00:06:51.100 --> 00:06:53.052 transforming what time gradients
NOTE Confidence: 0.580223618888889

00:06:53.052 --> 00:06:55.659 are shown here in the parking form.
NOTE Confidence: 0.580223618888889

00:06:55.660 --> 00:06:58.688 Let me just go around the cell here first.
NOTE Confidence: 0.580223618888889

00:06:58.688 --> 00:07:02.228 Is this mechanism here carbonic
NOTE Confidence: 0.580223618888889

00:07:02.230 --> 00:07:04.081 anhydrase mine specifically?
NOTE Confidence: 0.580223618888889

00:07:04.081 --> 00:07:06.549 But these kinds of.

NOTE Confidence: 0.825411373846154

00:07:08.690 --> 00:07:11.707 Instruments are used to basically take out

NOTE Confidence: 0.825411373846154

00:07:11.707 --> 00:07:14.260 department dioxide and water generated by

NOTE Confidence: 0.828720365714286

00:07:16.350 --> 00:07:19.129 oxidation and take them out and it

NOTE Confidence: 0.828720365714286

00:07:19.129 --> 00:07:21.261 basically takes them out and comes

NOTE Confidence: 0.828720365714286

00:07:21.261 --> 00:07:24.510 to bicarbonate and protons and which

NOTE Confidence: 0.828720365714286

00:07:24.510 --> 00:07:26.878 signifies the intracellular space.

NOTE Confidence: 0.828720365714286

00:07:26.880 --> 00:07:30.399 Then there is these channels at BCS and NC.

NOTE Confidence: 0.828720365714286

00:07:30.400 --> 00:07:33.280 Is which abbreviations are shown here,

NOTE Confidence: 0.828720365714286

00:07:33.280 --> 00:07:35.200 but the second time I'll just

NOTE Confidence: 0.828720365714286

00:07:35.200 --> 00:07:36.480 go through the abbreviations.

NOTE Confidence: 0.828720365714286

00:07:36.480 --> 00:07:38.835 These bring in both bicarbonate

NOTE Confidence: 0.828720365714286

00:07:38.835 --> 00:07:41.190 and sodium and this one.

NOTE Confidence: 0.828720365714286

00:07:41.190 --> 00:07:44.070 Runs in bicarbonate itself, right islands.

NOTE Confidence: 0.828720365714286

00:07:44.070 --> 00:07:48.190 Both of these contributed to a contribute to.

NOTE Confidence: 0.828720365714286

00:07:48.190 --> 00:07:51.890 Changing of the intracellular field.

NOTE Confidence: 0.828720365714286

00:07:51.890 --> 00:07:53.822 Maximo carboxylate transporters
NOTE Confidence: 0.828720365714286

00:07:53.822 --> 00:07:58.148 are those kinds and city one and
NOTE Confidence: 0.828720365714286

00:07:58.148 --> 00:08:00.438 NC 3-4 working opposite days.
NOTE Confidence: 0.828720365714286

00:08:00.440 --> 00:08:03.996 They bring in assets for NCT one
NOTE Confidence: 0.828720365714286

00:08:03.996 --> 00:08:08.009 and take out assets for actually 4
NOTE Confidence: 0.828720365714286

00:08:08.010 --> 00:08:12.110 altering hydrogen ion concentration.
NOTE Confidence: 0.828720365714286

00:08:12.110 --> 00:08:14.729 It's all specifically.
NOTE Confidence: 0.828720365714286

00:08:14.730 --> 00:08:16.656 Important one entity,
NOTE Confidence: 0.828720365714286

00:08:16.656 --> 00:08:19.224 one sodium proton exchanger,
NOTE Confidence: 0.828720365714286

00:08:19.230 --> 00:08:21.806 takes like for every proton taken out,
NOTE Confidence: 0.828720365714286

00:08:21.810 --> 00:08:25.154 brings in every brings in a sodium and
NOTE Confidence: 0.828720365714286

00:08:25.154 --> 00:08:29.918 that can alter the full time as well.
NOTE Confidence: 0.828720365714286

00:08:29.920 --> 00:08:33.520 These are ATP and ATP dependent,
NOTE Confidence: 0.828720365714286

00:08:33.520 --> 00:08:35.744 vascular full-time ATP ace,
NOTE Confidence: 0.828720365714286

00:08:35.744 --> 00:08:38.310 where you're bringing in or taking
NOTE Confidence: 0.828720365714286

00:08:38.310 --> 00:08:41.253 out protons to a city public service

NOTE Confidence: 0.828720365714286

00:08:41.253 --> 00:08:45.750 place as well as these acid.

NOTE Confidence: 0.828720365714286

00:08:45.750 --> 00:08:49.908 Sensing line channels as well as these

NOTE Confidence: 0.828720365714286

00:08:49.908 --> 00:08:52.590 epithelial specific certain channels.

NOTE Confidence: 0.828720365714286

00:08:52.590 --> 00:08:55.615 They also are known to affect more

NOTE Confidence: 0.828720365714286

00:08:55.615 --> 00:08:57.895 time but as well as sodium because a

NOTE Confidence: 0.828720365714286

00:08:57.895 --> 00:09:00.437 lot of things different channels as

NOTE Confidence: 0.828720365714286

00:09:00.437 --> 00:09:02.545 sodium gradients and therefore beans

NOTE Confidence: 0.828720365714286

00:09:02.545 --> 00:09:04.675 won't be repeated because these are

NOTE Confidence: 0.828720365714286

00:09:04.675 --> 00:09:07.009 the channels that I just talked about.

NOTE Confidence: 0.828720365714286

00:09:07.010 --> 00:09:08.660 But there are other mechanism.

NOTE Confidence: 0.828720365714286

00:09:08.660 --> 00:09:09.976 This is a channel that I just

NOTE Confidence: 0.828720365714286

00:09:09.976 --> 00:09:11.250 showed in the previous slide.

NOTE Confidence: 0.828720365714286

00:09:11.250 --> 00:09:14.148 See energy as well as the

NOTE Confidence: 0.828720365714286

00:09:14.148 --> 00:09:16.080 sort of important change.

NOTE Confidence: 0.828720365714286

00:09:16.080 --> 00:09:19.329 Are all of these have a role in altering

NOTE Confidence: 0.828720365714286

00:09:19.329 --> 00:09:22.900 the sodium level in the exercise of space?

NOTE Confidence: 0.828720365714286

00:09:22.900 --> 00:09:25.060 This particular channel, the NSX,

NOTE Confidence: 0.828720365714286

00:09:25.060 --> 00:09:27.272 the sodium counseling exchanger,

NOTE Confidence: 0.828720365714286

00:09:27.272 --> 00:09:29.484 it's exchanges sodium for

NOTE Confidence: 0.828720365714286

00:09:29.484 --> 00:09:31.939 calcium between the compartments.

NOTE Confidence: 0.828720365714286

00:09:31.940 --> 00:09:33.956 It's interesting, it was recently discovered,

NOTE Confidence: 0.828720365714286

00:09:33.960 --> 00:09:36.348 but in cancer specifically,

NOTE Confidence: 0.828720365714286

00:09:36.348 --> 00:09:39.333 this is actually need to.

NOTE Confidence: 0.828720365714286

00:09:39.340 --> 00:09:40.244 In addition,

NOTE Confidence: 0.828720365714286

00:09:40.244 --> 00:09:42.956 there is this additional new channels

NOTE Confidence: 0.828720365714286

00:09:42.960 --> 00:09:45.522 mentioned here that are specific to

NOTE Confidence: 0.828720365714286

00:09:45.522 --> 00:09:48.040 sodium regulation across the department.

NOTE Confidence: 0.828720365714286

00:09:48.040 --> 00:09:49.979 The most important one of this is

NOTE Confidence: 0.828720365714286

00:09:49.979 --> 00:09:52.059 probably a well known as the support.

NOTE Confidence: 0.828720365714286

00:09:52.060 --> 00:09:55.990 The sodium proton switches exchanging

NOTE Confidence: 0.828720365714286

00:09:55.990 --> 00:10:00.272 of sodium and potent potassium at the

NOTE Confidence: 0.828720365714286
00:10:00.272 --> 00:10:06.072 cost of ATP to basically maintain a balance.
NOTE Confidence: 0.828720365714286
00:10:06.072 --> 00:10:09.960 To keep resting potential.
NOTE Confidence: 0.828720365714286
00:10:09.960 --> 00:10:12.025 The same so that the cell can
NOTE Confidence: 0.828720365714286
00:10:12.025 --> 00:10:13.680 actually keep on doing that.
NOTE Confidence: 0.828720365714286
00:10:13.680 --> 00:10:15.440 It's designed to do so.
NOTE Confidence: 0.828720365714286
00:10:15.440 --> 00:10:19.144 These are the mechanisms that are in play.
NOTE Confidence: 0.828720365714286
00:10:19.150 --> 00:10:21.574 Glucose metabolism is key to all
NOTE Confidence: 0.828720365714286
00:10:21.574 --> 00:10:24.204 of these processes and the healthy
NOTE Confidence: 0.828720365714286
00:10:24.204 --> 00:10:27.125 miracle as blood drains in both
NOTE Confidence: 0.828720365714286
00:10:27.125 --> 00:10:30.416 glucose and oxygen in the form of
NOTE Confidence: 0.828720365714286
00:10:30.416 --> 00:10:32.642 oxyhemoglobin glucose is its transport
NOTE Confidence: 0.828720365714286
00:10:32.642 --> 00:10:34.857 is expedited by these transporters,
NOTE Confidence: 0.828720365714286
00:10:34.860 --> 00:10:37.170 but oxygen goes through just
NOTE Confidence: 0.828720365714286
00:10:37.170 --> 00:10:40.540 passive diffusion into the cell.
NOTE Confidence: 0.828720365714286
00:10:40.540 --> 00:10:42.056 Just breakdown appointments through
NOTE Confidence: 0.828720365714286

00:10:42.056 --> 00:10:44.787 the bike clinic steps and then further
NOTE Confidence: 0.828720365714286

00:10:44.787 --> 00:10:47.986 breakdown in in in the prep cycle
NOTE Confidence: 0.828720365714286

00:10:47.986 --> 00:10:50.740 of generating large amounts of ATP.
NOTE Confidence: 0.828720365714286

00:10:50.740 --> 00:10:52.404 All of these processes,
NOTE Confidence: 0.828720365714286

00:10:52.404 --> 00:10:54.484 generally small amounts of protons
NOTE Confidence: 0.828720365714286

00:10:54.484 --> 00:10:57.025 but also carbon dioxide water which
NOTE Confidence: 0.828720365714286

00:10:57.025 --> 00:10:58.258 I just mentioned.
NOTE Confidence: 0.828720365714286

00:10:58.260 --> 00:11:01.768 Carbonic anhydrase has a has a role in in,
NOTE Confidence: 0.828720365714286

00:11:01.768 --> 00:11:04.960 in, in taking out these these these products.
NOTE Confidence: 0.828720365714286

00:11:04.960 --> 00:11:06.476 So this is a.
NOTE Confidence: 0.828720365714286

00:11:06.476 --> 00:11:09.210 Complete oxidation of glucose if you will,
NOTE Confidence: 0.828720365714286

00:11:09.210 --> 00:11:11.580 but even under normal conditions
NOTE Confidence: 0.9116335333333333

00:11:11.580 --> 00:11:12.720 there is some.
NOTE Confidence: 0.7868149483333333

00:11:16.200 --> 00:11:20.376 Less oxidation than expected from theory,
NOTE Confidence: 0.7868149483333333

00:11:20.380 --> 00:11:23.075 where some of the glucose is actually
NOTE Confidence: 0.7868149483333333

00:11:23.075 --> 00:11:24.880 shunted towards biosynthetic processes,

NOTE Confidence: 0.786814948333333
00:11:24.880 --> 00:11:29.446 but some of the invoices actually.
NOTE Confidence: 0.786814948333333
00:11:29.450 --> 00:11:32.650 Excluded in terms of lactate by the public.
NOTE Confidence: 0.786814948333333
00:11:32.650 --> 00:11:35.585 Feeds on CTV's that you
NOTE Confidence: 0.786814948333333
00:11:35.585 --> 00:11:37.346 have mentioned earlier.
NOTE Confidence: 0.786814948333333
00:11:37.350 --> 00:11:40.380 A lot of the protons generated are removed.
NOTE Confidence: 0.786814948333333
00:11:40.380 --> 00:11:42.930 As I said from these different
NOTE Confidence: 0.786814948333333
00:11:42.930 --> 00:11:45.013 mechanisms which I mentioned me
NOTE Confidence: 0.786814948333333
00:11:45.013 --> 00:11:47.329 cheese also about the heart races.
NOTE Confidence: 0.786814948333333
00:11:47.330 --> 00:11:51.200 But if cancer and the unhealthy durable the.
NOTE Confidence: 0.786814948333333
00:11:51.200 --> 00:11:53.660 A lot of dysfunction happens in
NOTE Confidence: 0.786814948333333
00:11:53.660 --> 00:11:56.318 terms of amount of bike policies,
NOTE Confidence: 0.786814948333333
00:11:56.320 --> 00:11:58.550 which is the amount of
NOTE Confidence: 0.786814948333333
00:11:58.550 --> 00:11:59.888 oxidation that happens.
NOTE Confidence: 0.786814948333333
00:11:59.890 --> 00:12:02.210 And therefore some of these
NOTE Confidence: 0.786814948333333
00:12:02.210 --> 00:12:03.882 there will be glycolytic.
NOTE Confidence: 0.786814948333333

00:12:03.882 --> 00:12:06.390 Steps are augmented to the point.
NOTE Confidence: 0.786814948333333

00:12:06.390 --> 00:12:09.348 Where these machinery's that I speak
NOTE Confidence: 0.786814948333333

00:12:09.348 --> 00:12:11.830 just mentioned with carbonic and
NOTE Confidence: 0.786814948333333

00:12:11.830 --> 00:12:14.558 hybrid sister upregulated in NCT 4?
NOTE Confidence: 0.786814948333333

00:12:14.558 --> 00:12:17.360 Is that up regulated to handle
NOTE Confidence: 0.786814948333333

00:12:17.454 --> 00:12:20.869 exclusion of lactate more efficiently,
NOTE Confidence: 0.786814948333333

00:12:20.870 --> 00:12:24.566 but also in terms of the NET,
NOTE Confidence: 0.786814948333333

00:12:24.570 --> 00:12:27.814 which is also up regulated to alter the
NOTE Confidence: 0.786814948333333

00:12:27.814 --> 00:12:31.083 whole time in the access center space.
NOTE Confidence: 0.786814948333333

00:12:31.090 --> 00:12:31.760 We vacuumed.
NOTE Confidence: 0.896359014285714

00:12:34.850 --> 00:12:36.908 Along with some of the same mechanism,
NOTE Confidence: 0.896359014285714

00:12:36.910 --> 00:12:39.766 the same machinery or additional machinery,
NOTE Confidence: 0.896359014285714

00:12:39.770 --> 00:12:43.151 you can also experience a lot of
NOTE Confidence: 0.896359014285714

00:12:43.151 --> 00:12:44.932 imbalances in a certain environment,
NOTE Confidence: 0.896359014285714

00:12:44.932 --> 00:12:47.279 but key player as I just mentioned
NOTE Confidence: 0.896359014285714

00:12:47.279 --> 00:12:49.325 is the mutation of the NSX,

NOTE Confidence: 0.896359014285714
00:12:49.330 --> 00:12:51.430 which happens which is most
NOTE Confidence: 0.896359014285714
00:12:51.430 --> 00:12:53.110 recently discovered in cancer,
NOTE Confidence: 0.896359014285714
00:12:53.110 --> 00:12:56.426 but also the fact that there
NOTE Confidence: 0.896359014285714
00:12:56.426 --> 00:12:59.530 is actually downregulation of
NOTE Confidence: 0.896359014285714
00:12:59.530 --> 00:13:03.920 oxidation within a cancer cells.
NOTE Confidence: 0.896359014285714
00:13:03.920 --> 00:13:11.036 Reduce potassium sodium is also an important
NOTE Confidence: 0.896359014285714
00:13:11.036 --> 00:13:14.970 role of causing these sodium imbalances as.
NOTE Confidence: 0.896359014285714
00:13:14.970 --> 00:13:16.617 And it's culture.
NOTE Confidence: 0.896359014285714
00:13:16.617 --> 00:13:20.970 So this is the unhealthy miracle and our.
NOTE Confidence: 0.896359014285714
00:13:20.970 --> 00:13:24.323 Our role is to understand and observe
NOTE Confidence: 0.896359014285714
00:13:24.323 --> 00:13:27.392 these the impact of the altered proton
NOTE Confidence: 0.896359014285714
00:13:27.392 --> 00:13:29.006 as well as transgender, Ingrid.
NOTE Confidence: 0.896359014285714
00:13:29.006 --> 00:13:31.442 So tumors are highly like little
NOTE Confidence: 0.896359014285714
00:13:31.442 --> 00:13:34.134 even when off, well oxygenated,
NOTE Confidence: 0.896359014285714
00:13:34.134 --> 00:13:37.819 and this aerobic glycolysis phenotype.
NOTE Confidence: 0.896359014285714

00:13:37.820 --> 00:13:39.772 Enables enabled by metabolism.
NOTE Confidence: 0.896359014285714

00:13:39.772 --> 00:13:41.236 Different nutrients generates
NOTE Confidence: 0.896359014285714

00:13:41.236 --> 00:13:43.733 lots of their civic products
NOTE Confidence: 0.896359014285714

00:13:43.733 --> 00:13:45.665 that are extremely deficient.
NOTE Confidence: 0.896359014285714

00:13:45.670 --> 00:13:46.444 For example,
NOTE Confidence: 0.896359014285714

00:13:46.444 --> 00:13:48.766 even carbon dioxide and water generated
NOTE Confidence: 0.896359014285714

00:13:48.766 --> 00:13:50.469 from oxidative metabolism are,
NOTE Confidence: 0.896359014285714

00:13:50.470 --> 00:13:51.334 you know,
NOTE Confidence: 0.896359014285714

00:13:51.334 --> 00:13:53.062 they contribute to certification
NOTE Confidence: 0.896359014285714

00:13:53.062 --> 00:13:55.369 of the interstitial space by these
NOTE Confidence: 0.896359014285714

00:13:55.370 --> 00:14:00.078 these anionic exchangers like.
NOTE Confidence: 0.896359014285714

00:14:00.080 --> 00:14:00.450 Invite.
NOTE Confidence: 0.60703224325

00:14:02.680 --> 00:14:04.315 Interstitial acidosis actually
NOTE Confidence: 0.60703224325

00:14:04.315 --> 00:14:07.040 helps with tumor cell invasion.
NOTE Confidence: 0.60703224325

00:14:07.040 --> 00:14:09.250 They they actually did break
NOTE Confidence: 0.60703224325

00:14:09.250 --> 00:14:10.576 the interstitial matrix,

NOTE Confidence: 0.60703224325

00:14:10.580 --> 00:14:14.360 and they also promote angiogenesis

NOTE Confidence: 0.60703224325

00:14:14.360 --> 00:14:18.308 while suppressing entry. Sense.

NOTE Confidence: 0.60703224325

00:14:18.308 --> 00:14:21.727 So this is an example from Bob

NOTE Confidence: 0.60703224325

00:14:21.727 --> 00:14:25.976 Giles work where it is shown that

NOTE Confidence: 0.60703224325

00:14:25.976 --> 00:14:28.442 whenever there is use acidification,

NOTE Confidence: 0.60703224325

00:14:28.442 --> 00:14:31.988 this is done in a culture system

NOTE Confidence: 0.60703224325

00:14:31.988 --> 00:14:35.060 where there's reduce acidification,

NOTE Confidence: 0.60703224325

00:14:35.060 --> 00:14:37.915 there is enhanced invasion of

NOTE Confidence: 0.60703224325

00:14:37.915 --> 00:14:40.660 cells in terms of timber growth.

NOTE Confidence: 0.60703224325

00:14:40.660 --> 00:14:42.335 This is an example where

NOTE Confidence: 0.60703224325

00:14:42.335 --> 00:14:43.888 you study shown in situ,

NOTE Confidence: 0.60703224325

00:14:43.888 --> 00:14:45.532 but in people evidence for this

NOTE Confidence: 0.60703224325

00:14:45.532 --> 00:14:47.197 from our lab and other labs,

NOTE Confidence: 0.60703224325

00:14:47.200 --> 00:14:50.628 so security is absolute.

NOTE Confidence: 0.60703224325

00:14:50.630 --> 00:14:53.126 Impact with the altered transplant in

NOTE Confidence: 0.60703224325

00:14:53.126 --> 00:14:55.430 sodium gradient normal cells maintain.

NOTE Confidence: 0.60703224325

00:14:55.430 --> 00:14:58.340 Hyperpolarized membrane potential.

NOTE Confidence: 0.60703224325

00:14:58.340 --> 00:15:01.358 But before I see member interventional

NOTE Confidence: 0.60703224325

00:15:01.358 --> 00:15:05.776 and non excitable cells is linked to

NOTE Confidence: 0.60703224325

00:15:05.776 --> 00:15:09.662 their proliferation of point to this in

NOTE Confidence: 0.60703224325

00:15:09.662 --> 00:15:11.770 in the next slide a little bit more.

NOTE Confidence: 0.60703224325

00:15:11.770 --> 00:15:14.962 In fact, even in mean cells consensus

NOTE Confidence: 0.60703224325

00:15:14.962 --> 00:15:17.370 in the interstitial in the loop.

NOTE Confidence: 0.60703224325

00:15:17.370 --> 00:15:17.848 Therefore,

NOTE Confidence: 0.60703224325

00:15:17.848 --> 00:15:20.238 salinity of the interstitial and

NOTE Confidence: 0.60703224325

00:15:20.238 --> 00:15:22.710 intracellular compartments may be crucial.

NOTE Confidence: 0.60703224325

00:15:22.710 --> 00:15:26.448 As has been pointed out by recent.

NOTE Confidence: 0.60703224325

00:15:26.450 --> 00:15:28.622 Work that may be important for

NOTE Confidence: 0.60703224325

00:15:28.622 --> 00:15:30.070 early diagnosis of cancer,

NOTE Confidence: 0.60703224325

00:15:30.070 --> 00:15:32.314 but also maybe contracting

NOTE Confidence: 0.60703224325

00:15:32.314 --> 00:15:33.997 in cancer treatments.

NOTE Confidence: 0.60703224325
00:15:34.000 --> 00:15:35.816 So this point, this light points this out.
NOTE Confidence: 0.60703224325
00:15:35.820 --> 00:15:38.277 This is the scale of membrane potential.
NOTE Confidence: 0.60703224325
00:15:38.280 --> 00:15:40.630 On the bottom are these
NOTE Confidence: 0.60703224325
00:15:40.630 --> 00:15:42.040 non proliferating cells?
NOTE Confidence: 0.60703224325
00:15:42.040 --> 00:15:43.672 These are real cells,
NOTE Confidence: 0.60703224325
00:15:43.672 --> 00:15:44.488 neuronal cells.
NOTE Confidence: 0.60703224325
00:15:44.490 --> 00:15:47.980 They have a very hyperpolarized
NOTE Confidence: 0.60703224325
00:15:47.980 --> 00:15:50.046 membrane potential equation which
NOTE Confidence: 0.60703224325
00:15:50.046 --> 00:15:51.711 takes into account sodium and
NOTE Confidence: 0.60703224325
00:15:51.711 --> 00:15:53.840 the poor at concentrations up.
NOTE Confidence: 0.60703224325
00:15:53.840 --> 00:15:55.176 Here are the perfect.
NOTE Confidence: 0.60703224325
00:15:55.176 --> 00:15:57.180 Or looks writing cells which are
NOTE Confidence: 0.60703224325
00:15:57.248 --> 00:15:59.438 non tumor cells but the membrane
NOTE Confidence: 0.60703224325
00:15:59.438 --> 00:16:01.301 potential measure of tumor cells
NOTE Confidence: 0.60703224325
00:16:01.301 --> 00:16:03.317 in the rieti of different kinds.
NOTE Confidence: 0.60703224325

00:16:03.320 --> 00:16:06.848 You see they right up here in the
NOTE Confidence: 0.60703224325

00:16:06.848 --> 00:16:09.596 depolarized level. So in essence.
NOTE Confidence: 0.60703224325

00:16:09.596 --> 00:16:13.328 What a lot about solutions from
NOTE Confidence: 0.60703224325

00:16:13.328 --> 00:16:17.500 various groups have shown is that.
NOTE Confidence: 0.60703224325

00:16:17.500 --> 00:16:19.752 The week transmembrane sodium
NOTE Confidence: 0.60703224325

00:16:19.752 --> 00:16:22.004 gradient maintaining a depolarized
NOTE Confidence: 0.60703224325

00:16:22.004 --> 00:16:23.973 membrane potential is actually
NOTE Confidence: 0.60703224325

00:16:23.973 --> 00:16:26.289 necessary for these cells to survive
NOTE Confidence: 0.60703224325

00:16:26.289 --> 00:16:28.476 in their altered environment that
NOTE Confidence: 0.60703224325

00:16:28.476 --> 00:16:30.745 they create for their survival.
NOTE Confidence: 0.60703224325

00:16:30.745 --> 00:16:32.200 Update at the.
NOTE Confidence: 0.60703224325

00:16:32.200 --> 00:16:36.030 Cost of normal cells that they're replacing.
NOTE Confidence: 0.60703224325

00:16:36.030 --> 00:16:38.970 Whereas you know these normal cells,
NOTE Confidence: 0.60703224325

00:16:38.970 --> 00:16:40.394 especially in the brain,
NOTE Confidence: 0.60703224325

00:16:40.394 --> 00:16:41.106 maintain strong,
NOTE Confidence: 0.60703224325

00:16:41.110 --> 00:16:42.226 transmembrane certain buildings

NOTE Confidence: 0.60703224325

00:16:42.226 --> 00:16:44.830 and they may do so by maintaining

NOTE Confidence: 0.60703224325

00:16:44.896 --> 00:16:46.100 their hyperpolarized.

NOTE Confidence: 0.908159307142857

00:16:48.640 --> 00:16:51.937 So these are the hallmarks of cancer,

NOTE Confidence: 0.908159307142857

00:16:51.940 --> 00:16:54.847 our goal, and my goal in the next few

NOTE Confidence: 0.908159307142857

00:16:54.847 --> 00:16:57.446 minutes is to show that you can employ

NOTE Confidence: 0.908159307142857

00:16:57.446 --> 00:17:00.176 sodium and proton imaging methods

NOTE Confidence: 0.908159307142857

00:17:00.176 --> 00:17:04.219 to actually observe 2 properties,

NOTE Confidence: 0.908159307142857

00:17:04.220 --> 00:17:07.358 invasion and proliferation of cancer cells

NOTE Confidence: 0.908159307142857

00:17:07.360 --> 00:17:11.380 by using proton and imaging perspective.

NOTE Confidence: 0.908159307142857

00:17:11.380 --> 00:17:13.235 We talked a little bit about that.

NOTE Confidence: 0.908159307142857

00:17:13.240 --> 00:17:14.908 I'm sure this method is quite

NOTE Confidence: 0.908159307142857

00:17:14.908 --> 00:17:15.742 familiar with most.

NOTE Confidence: 0.288172156666667

00:17:21.120 --> 00:17:22.128 Slash house light.

NOTE Confidence: 0.417400417333333

00:17:38.200 --> 00:17:39.049 Turns out that.

NOTE Confidence: 0.2631551125

00:17:44.990 --> 00:17:49.358 In like one step. Slide disappeared, yeah.

NOTE Confidence: 0.2631551125

00:17:49.360 --> 00:17:51.862 I realized that it just didn't like 1 slide.
NOTE Confidence: 0.846737995714286

00:17:54.920 --> 00:17:56.159 Do you wanna stop sharing and start
NOTE Confidence: 0.846737995714286

00:17:56.159 --> 00:17:57.600 again or is that what you're doing?
NOTE Confidence: 0.81298438125

00:17:57.900 --> 00:17:59.790 Yeah, I'm trying to do that right now, OK?
NOTE Confidence: 0.10258365

00:18:01.270 --> 00:18:03.860 OK, so I'll skip that slide.
NOTE Confidence: 0.29788578

00:18:10.250 --> 00:18:12.447 And see if I can get from that.
NOTE Confidence: 0.9386621

00:18:15.450 --> 00:18:20.790 So the slide that I unfortunately had that.
NOTE Confidence: 0.9386621

00:18:20.790 --> 00:18:23.934 You know it bounced me out of PowerPoint.
NOTE Confidence: 0.9386621

00:18:23.940 --> 00:18:27.360 Basically this describes a key late.
NOTE Confidence: 0.9386621

00:18:27.360 --> 00:18:30.112 That is the design structure of most contrast
NOTE Confidence: 0.9386621

00:18:30.112 --> 00:18:32.266 agents that is used in the preferable
NOTE Confidence: 0.9386621

00:18:32.266 --> 00:18:35.052 design is where you take a gadolinium.
NOTE Confidence: 0.9386621

00:18:35.060 --> 00:18:38.228 Mine is very car magnetic and you
NOTE Confidence: 0.9386621

00:18:38.228 --> 00:18:41.522 use that to reduce its toxicity
NOTE Confidence: 0.9386621

00:18:41.522 --> 00:18:44.240 Yuzuki late with donating.
NOTE Confidence: 0.9386621

00:18:44.240 --> 00:18:47.000 Components like oxygen atoms that would

NOTE Confidence: 0.9386621

00:18:47.000 --> 00:18:49.770 provide the stability for conjugation,

NOTE Confidence: 0.9386621

00:18:49.770 --> 00:18:51.591 reducing discovery toxicity

NOTE Confidence: 0.9386621

00:18:51.591 --> 00:18:54.019 of the metal iron.

NOTE Confidence: 0.9386621

00:18:54.020 --> 00:18:56.799 But discriminating iron is some of the

NOTE Confidence: 0.9386621

00:18:56.799 --> 00:18:59.430 key of the types of imaging observations

NOTE Confidence: 0.9386621

00:18:59.430 --> 00:19:01.915 that I'm going to show you about.

NOTE Confidence: 0.9386621

00:19:01.920 --> 00:19:03.852 So this is essentially a proton

NOTE Confidence: 0.9386621

00:19:03.852 --> 00:19:06.199 spectrum of a key late like this.

NOTE Confidence: 0.9386621

00:19:06.200 --> 00:19:09.336 This is a it's called appear TP molecule.

NOTE Confidence: 0.9386621

00:19:09.340 --> 00:19:11.670 It's basically a molecule that

NOTE Confidence: 0.9386621

00:19:11.670 --> 00:19:13.534 contains multiple phosphinate groups,

NOTE Confidence: 0.9386621

00:19:13.540 --> 00:19:15.570 much like phosphonates that exist

NOTE Confidence: 0.9386621

00:19:15.570 --> 00:19:17.950 in molecules like ATP and ADP.

NOTE Confidence: 0.81158357

00:19:18.480 --> 00:19:19.650 So this is a very

NOTE Confidence: 0.860093169166667

00:19:20.020 --> 00:19:22.306 common diamagnetic range of signals that

NOTE Confidence: 0.860093169166667

00:19:22.306 --> 00:19:24.729 you would see emanating for different.
NOTE Confidence: 0.860093169166667

00:19:24.730 --> 00:19:27.586 Protons, the non exchangeable protons that
NOTE Confidence: 0.860093169166667

00:19:27.586 --> 00:19:31.154 exist in these carbons as well as the
NOTE Confidence: 0.860093169166667

00:19:31.154 --> 00:19:33.530 carbons existing in these pendant arms.
NOTE Confidence: 0.9649444675

00:19:35.700 --> 00:19:37.340 By the way, I point out that these
NOTE Confidence: 0.9649444675

00:19:37.340 --> 00:19:40.036 phosphates on this on a molecule like this.
NOTE Confidence: 0.9649444675

00:19:40.040 --> 00:19:42.290 These protons exchange with protons
NOTE Confidence: 0.9649444675

00:19:42.290 --> 00:19:45.321 of water and that kind of exchange
NOTE Confidence: 0.9649444675

00:19:45.321 --> 00:19:48.400 is actually a a a pH mediated
NOTE Confidence: 0.9649444675

00:19:48.400 --> 00:19:51.840 and and and therefore they are.
NOTE Confidence: 0.9649444675

00:19:51.840 --> 00:19:54.240 These molecules are essentially
NOTE Confidence: 0.9649444675

00:19:54.240 --> 00:19:57.692 create sensor much like ATP and
NOTE Confidence: 0.9649444675

00:19:57.692 --> 00:20:00.067 ADP is using phosphorus and.
NOTE Confidence: 0.9649444675

00:20:00.070 --> 00:20:02.728 So if you now collate this,
NOTE Confidence: 0.9649444675

00:20:02.730 --> 00:20:05.046 take this molecule and and complexes
NOTE Confidence: 0.9649444675

00:20:05.046 --> 00:20:06.590 with the paramagnetic metal.

NOTE Confidence: 0.9649444675

00:20:06.590 --> 00:20:07.343 In this case,

NOTE Confidence: 0.9649444675

00:20:07.343 --> 00:20:08.347 I'm not using gadolinium,

NOTE Confidence: 0.9649444675

00:20:08.350 --> 00:20:11.942 but a fully am I and you essentially

NOTE Confidence: 0.9649444675

00:20:11.942 --> 00:20:14.108 caused this large expansion of the

NOTE Confidence: 0.9649444675

00:20:14.108 --> 00:20:16.385 same chemical shift that you see here

NOTE Confidence: 0.9649444675

00:20:16.385 --> 00:20:18.760 within a few partner million and that's

NOTE Confidence: 0.9649444675

00:20:18.760 --> 00:20:20.735 expanded by hundreds across people.

NOTE Confidence: 0.9649444675

00:20:20.740 --> 00:20:23.728 So these signals have no potential

NOTE Confidence: 0.9649444675

00:20:23.728 --> 00:20:26.650 overlap with other types of signals

NOTE Confidence: 0.9649444675

00:20:26.650 --> 00:20:28.870 that you may observe in vivo.

NOTE Confidence: 0.9649444675

00:20:28.870 --> 00:20:31.228 And this is the water signal.

NOTE Confidence: 0.9649444675

00:20:31.230 --> 00:20:33.396 And so this hyperfine shifted

NOTE Confidence: 0.9649444675

00:20:33.396 --> 00:20:36.026 signal has very unusual properties.

NOTE Confidence: 0.9649444675

00:20:36.030 --> 00:20:37.800 Basically, all it means is that

NOTE Confidence: 0.9649444675

00:20:37.800 --> 00:20:39.490 you can observe them quickly.

NOTE Confidence: 0.9649444675

00:20:39.490 --> 00:20:42.670 You can observe them under very
NOTE Confidence: 0.9649444675

00:20:42.670 --> 00:20:45.841 precarious in vivo situations that we
NOTE Confidence: 0.9649444675

00:20:45.841 --> 00:20:48.552 may experience the relaxation times are
NOTE Confidence: 0.9649444675

00:20:48.552 --> 00:20:51.180 so short because of the paramagnetic
NOTE Confidence: 0.9649444675

00:20:51.261 --> 00:20:53.276 environment that that these photons
NOTE Confidence: 0.9649444675

00:20:53.276 --> 00:20:56.729 are in create a very sensitive scenario.
NOTE Confidence: 0.9649444675

00:20:56.730 --> 00:20:57.714 That's most, importantly,
NOTE Confidence: 0.9649444675

00:20:57.714 --> 00:21:00.010 that the chemical shift of these signals,
NOTE Confidence: 0.9649444675

00:21:00.010 --> 00:21:01.150 not the amplitude,
NOTE Confidence: 0.9649444675

00:21:01.150 --> 00:21:02.290 of these signals.
NOTE Confidence: 0.9649444675

00:21:02.290 --> 00:21:05.175 But how these signals are
NOTE Confidence: 0.9649444675

00:21:05.175 --> 00:21:07.500 located and how they shift?
NOTE Confidence: 0.9649444675

00:21:07.500 --> 00:21:10.356 Is the readout that we observe again,
NOTE Confidence: 0.9649444675

00:21:10.360 --> 00:21:13.177 so this is a molecule which is the sensor.
NOTE Confidence: 0.9649444675

00:21:13.180 --> 00:21:15.130 So if you change the
NOTE Confidence: 0.9649444675

00:21:15.130 --> 00:21:16.690 environment of the sensor.

NOTE Confidence: 0.9649444675

00:21:16.690 --> 00:21:19.070 The structure of the molecule will change

NOTE Confidence: 0.9649444675

00:21:19.070 --> 00:21:22.387 and as the structure of the molecule changes.

NOTE Confidence: 0.9649444675

00:21:22.390 --> 00:21:25.204 What you then read out that structural

NOTE Confidence: 0.9649444675

00:21:25.204 --> 00:21:27.659 changes from the chemical change.

NOTE Confidence: 0.9649444675

00:21:27.660 --> 00:21:29.880 And so this is encapsulated here.

NOTE Confidence: 0.9649444675

00:21:29.880 --> 00:21:31.698 This is a molecule that we

NOTE Confidence: 0.9649444675

00:21:31.698 --> 00:21:33.480 are using as our sensor.

NOTE Confidence: 0.9649444675

00:21:33.480 --> 00:21:36.640 These are the types of signals that we

NOTE Confidence: 0.9649444675

00:21:36.640 --> 00:21:39.715 observe using this as an example 86 proton.

NOTE Confidence: 0.9649444675

00:21:39.720 --> 00:21:41.520 It has a pH sensitivity,

NOTE Confidence: 0.9649444675

00:21:41.520 --> 00:21:43.185 but obviously any molecule reports

NOTE Confidence: 0.9649444675

00:21:43.185 --> 00:21:44.850 environment by changes like these

NOTE Confidence: 0.9649444675

00:21:44.908 --> 00:21:46.612 molecules have or molecules like this

NOTE Confidence: 0.9649444675

00:21:46.612 --> 00:21:48.639 have very very short relaxation times.

NOTE Confidence: 0.9649444675

00:21:48.640 --> 00:21:50.932 So you can observe them quickly

NOTE Confidence: 0.9649444675

00:21:50.932 --> 00:21:52.921 and therefore imaging these have
NOTE Confidence: 0.9649444675

00:21:52.921 --> 00:21:55.508 been possible and the readout from
NOTE Confidence: 0.9649444675

00:21:55.508 --> 00:21:58.060 them in terms of chemical shift is.
NOTE Confidence: 0.9649444675

00:21:58.060 --> 00:22:01.708 Not confounded by other overlapping signals.
NOTE Confidence: 0.9649444675

00:22:01.710 --> 00:22:04.572 So this is an in vitro example of this
NOTE Confidence: 0.9649444675

00:22:04.572 --> 00:22:07.506 kind of work from my colleague Dan
NOTE Confidence: 0.9649444675

00:22:07.506 --> 00:22:10.950 Employment and then this method is.
NOTE Confidence: 0.9649444675

00:22:10.950 --> 00:22:12.698 Paul by sensor imaging,
NOTE Confidence: 0.9649444675

00:22:12.698 --> 00:22:15.273 redundant deviation shifts, birds for short.
NOTE Confidence: 0.9649444675

00:22:15.273 --> 00:22:17.799 Essentially showing you that in these
NOTE Confidence: 0.9649444675

00:22:17.799 --> 00:22:21.058 two phantoms which have very different pH,
NOTE Confidence: 0.9649444675

00:22:21.060 --> 00:22:23.400 you can read out the pH with high confidence
NOTE Confidence: 0.9649444675

00:22:23.400 --> 00:22:25.317 even if you change the temperature.
NOTE Confidence: 0.9649444675

00:22:25.320 --> 00:22:27.168 So you can essentially
NOTE Confidence: 0.9649444675

00:22:27.168 --> 00:22:29.478 give these two things out.
NOTE Confidence: 0.9649444675

00:22:29.480 --> 00:22:30.420 Simultaneously,

NOTE Confidence: 0.9649444675

00:22:30.420 --> 00:22:33.261 the key thing is is that this is

NOTE Confidence: 0.9649444675

00:22:33.261 --> 00:22:36.059 not like most imaging contrast.

NOTE Confidence: 0.9649444675

00:22:36.060 --> 00:22:38.670 This contrast is not based on

NOTE Confidence: 0.9649444675

00:22:38.670 --> 00:22:41.659 the amount of agent that you have

NOTE Confidence: 0.9649444675

00:22:41.660 --> 00:22:43.500 in in the given compartment,

NOTE Confidence: 0.9649444675

00:22:43.500 --> 00:22:44.980 but really their chemical shift.

NOTE Confidence: 0.9649444675

00:22:44.980 --> 00:22:47.140 So it's it's a readout that's

NOTE Confidence: 0.9649444675

00:22:47.140 --> 00:22:48.220 independent of concentration,

NOTE Confidence: 0.9649444675

00:22:48.220 --> 00:22:50.324 and so using this method we've

NOTE Confidence: 0.9649444675

00:22:50.324 --> 00:22:52.836 been able to apply it to look at

NOTE Confidence: 0.9649444675

00:22:52.840 --> 00:22:54.154 the cancer environment,

NOTE Confidence: 0.9649444675

00:22:54.154 --> 00:22:57.220 specifically the the pH in the extracellular

NOTE Confidence: 0.734225631818182

00:22:57.293 --> 00:22:59.430 space, and a variety of different.

NOTE Confidence: 0.734225631818182

00:22:59.430 --> 00:23:02.255 Scenarios these these are examples

NOTE Confidence: 0.734225631818182

00:23:02.255 --> 00:23:04.554 from breaking specifically shown for

NOTE Confidence: 0.734225631818182

00:23:04.554 --> 00:23:06.366 two different types of tumors here,
NOTE Confidence: 0.734225631818182

00:23:06.370 --> 00:23:09.370 but you can note and appreciate the acidity.
NOTE Confidence: 0.734225631818182

00:23:09.370 --> 00:23:13.306 Acidity within the tumor poor as shown here.
NOTE Confidence: 0.734225631818182

00:23:13.310 --> 00:23:17.786 Core being identified by the line
NOTE Confidence: 0.734225631818182

00:23:17.790 --> 00:23:20.954 that shows up in the MRI contrast.
NOTE Confidence: 0.734225631818182

00:23:20.960 --> 00:23:22.748 But you can also appreciate this
NOTE Confidence: 0.734225631818182

00:23:22.748 --> 00:23:24.358 extended area of a certification
NOTE Confidence: 0.734225631818182

00:23:24.358 --> 00:23:26.815 for this tumor and not that tumor,
NOTE Confidence: 0.734225631818182

00:23:26.820 --> 00:23:29.004 and that has to do with the
NOTE Confidence: 0.734225631818182

00:23:29.004 --> 00:23:30.660 how evasive this tumor is,
NOTE Confidence: 0.734225631818182

00:23:30.660 --> 00:23:32.500 and using cellular markers,
NOTE Confidence: 0.734225631818182

00:23:32.500 --> 00:23:34.800 you can corroborate that funding,
NOTE Confidence: 0.734225631818182

00:23:34.800 --> 00:23:36.762 so this goes back to the
NOTE Confidence: 0.734225631818182

00:23:36.762 --> 00:23:38.780 point that our pH readout,
NOTE Confidence: 0.734225631818182

00:23:38.780 --> 00:23:40.716 so this is a case of a a
NOTE Confidence: 0.734225631818182

00:23:40.716 --> 00:23:42.380 very non invasive tumor,

NOTE Confidence: 0.734225631818182

00:23:42.380 --> 00:23:47.364 versus this one is tumors invade and this.

NOTE Confidence: 0.734225631818182

00:23:47.370 --> 00:23:49.462 Invasion if you will.

NOTE Confidence: 0.734225631818182

00:23:49.462 --> 00:23:52.600 I we believe is essentially preconditioning

NOTE Confidence: 0.734225631818182

00:23:52.686 --> 00:23:56.230 for the expansion of this tumor within time.

NOTE Confidence: 0.734225631818182

00:23:56.230 --> 00:23:58.030 For these two specific cases,

NOTE Confidence: 0.734225631818182

00:23:58.030 --> 00:24:02.958 here in the 2nd and R2, but not the help.

NOTE Confidence: 0.734225631818182

00:24:02.960 --> 00:24:05.632 So talked about a little bit about what

NOTE Confidence: 0.734225631818182

00:24:05.632 --> 00:24:08.466 we do with the Proton imaging part to

NOTE Confidence: 0.734225631818182

00:24:08.466 --> 00:24:11.676 read up pH and that uses the proton nucleus,

NOTE Confidence: 0.734225631818182

00:24:11.680 --> 00:24:12.145 right?

NOTE Confidence: 0.734225631818182

00:24:12.145 --> 00:24:14.935 This is a very highly sensitive

NOTE Confidence: 0.734225631818182

00:24:14.940 --> 00:24:17.124 nucleus to observe because with the

NOTE Confidence: 0.734225631818182

00:24:17.124 --> 00:24:18.580 hygiene gentlemen medical issue.

NOTE Confidence: 0.734225631818182

00:24:18.580 --> 00:24:21.316 But what I'm going to talk about next

NOTE Confidence: 0.734225631818182

00:24:21.316 --> 00:24:24.506 is the sodium imaging part which has

NOTE Confidence: 0.734225631818182

00:24:24.506 --> 00:24:27.224 a lower gyromagnetic ratio but aided
NOTE Confidence: 0.734225631818182

00:24:27.224 --> 00:24:30.320 by the fact that we are looking at.
NOTE Confidence: 0.734225631818182

00:24:30.320 --> 00:24:33.176 You know our product nucleus we are.
NOTE Confidence: 0.734225631818182

00:24:33.180 --> 00:24:36.312 So we can benefit a little bit from the
NOTE Confidence: 0.734225631818182

00:24:36.312 --> 00:24:39.126 certain relaxation times of this nucleus.
NOTE Confidence: 0.734225631818182

00:24:39.126 --> 00:24:41.940 So that's kind of where we are.
NOTE Confidence: 0.734225631818182

00:24:41.940 --> 00:24:44.614 Our basic rationale for this type of
NOTE Confidence: 0.734225631818182

00:24:44.614 --> 00:24:46.584 experiment is that the problem that
NOTE Confidence: 0.734225631818182

00:24:46.584 --> 00:24:48.900 we face is that the sodium signal,
NOTE Confidence: 0.734225631818182

00:24:48.900 --> 00:24:52.952 whether looking at the the interstitial
NOTE Confidence: 0.734225631818182

00:24:52.952 --> 00:24:55.000 or the intercellular pool,
NOTE Confidence: 0.734225631818182

00:24:55.000 --> 00:24:56.602 signals they overlap.
NOTE Confidence: 0.734225631818182

00:24:56.602 --> 00:24:58.738 They're not chemically different,
NOTE Confidence: 0.734225631818182

00:24:58.740 --> 00:25:00.440 and therefore the total signal
NOTE Confidence: 0.734225631818182

00:25:00.440 --> 00:25:02.677 you observe is is a representative
NOTE Confidence: 0.734225631818182

00:25:02.677 --> 00:25:04.958 of these two types, etc.

NOTE Confidence: 0.734225631818182

00:25:04.958 --> 00:25:07.954 Our expectation is that somehow we can

NOTE Confidence: 0.734225631818182

00:25:07.954 --> 00:25:10.729 separate the two and that separation.

NOTE Confidence: 0.734225631818182

00:25:10.730 --> 00:25:13.260 Will allow us to look at things

NOTE Confidence: 0.734225631818182

00:25:13.260 --> 00:25:15.540 like the transmembrane great.

NOTE Confidence: 0.734225631818182

00:25:15.540 --> 00:25:17.268 So the idea stemmed from work

NOTE Confidence: 0.734225631818182

00:25:17.268 --> 00:25:18.840 that existed in the field,

NOTE Confidence: 0.734225631818182

00:25:18.840 --> 00:25:21.736 but the advanced it in the last few

NOTE Confidence: 0.734225631818182

00:25:21.736 --> 00:25:25.817 years is that if we have a polyanionic.

NOTE Confidence: 0.734225631818182

00:25:25.820 --> 00:25:26.921 Our magnetic agent,

NOTE Confidence: 0.734225631818182

00:25:26.921 --> 00:25:29.950 much like pet agents that I've talked about.

NOTE Confidence: 0.734225631818182

00:25:29.950 --> 00:25:32.794 And we take a sodium ion because

NOTE Confidence: 0.734225631818182

00:25:32.794 --> 00:25:34.250 of its negative charge.

NOTE Confidence: 0.734225631818182

00:25:34.250 --> 00:25:37.430 It's attracted to it and there

NOTE Confidence: 0.734225631818182

00:25:37.430 --> 00:25:40.666 is superbound bounding of some of

NOTE Confidence: 0.734225631818182

00:25:40.666 --> 00:25:43.720 these ions because of the negative.

NOTE Confidence: 0.734225631818182

00:25:43.720 --> 00:25:46.492 Target of this agents and we have
NOTE Confidence: 0.734225631818182

00:25:46.492 --> 00:25:49.045 some exchange of free sodium with
NOTE Confidence: 0.734225631818182

00:25:49.045 --> 00:25:51.175 this sort of bound sodium,
NOTE Confidence: 0.734225631818182

00:25:51.180 --> 00:25:54.880 and if that exchange happens.
NOTE Confidence: 0.734225631818182

00:25:54.880 --> 00:25:58.169 Fast enough that we can reflect the
NOTE Confidence: 0.734225631818182

00:25:58.169 --> 00:26:00.863 shifting of the sodium signal from
NOTE Confidence: 0.734225631818182

00:26:00.863 --> 00:26:04.279 a from this process to reflect the
NOTE Confidence: 0.734225631818182

00:26:04.280 --> 00:26:06.370 true 2 compartments of service.
NOTE Confidence: 0.734225631818182

00:26:06.370 --> 00:26:07.423 So in essence,
NOTE Confidence: 0.734225631818182

00:26:07.423 --> 00:26:11.250 what we do and this is our rationale take.
NOTE Confidence: 0.734225631818182

00:26:11.250 --> 00:26:13.378 Before we add an agent like this,
NOTE Confidence: 0.734225631818182

00:26:13.380 --> 00:26:15.828 this is the total signal we will look here.
NOTE Confidence: 0.734225631818182

00:26:15.830 --> 00:26:18.734 And when we inject or introduce
NOTE Confidence: 0.734225631818182

00:26:18.734 --> 00:26:21.768 an agent like this because it's so
NOTE Confidence: 0.734225631818182

00:26:21.768 --> 00:26:23.964 negative and it can attract positive
NOTE Confidence: 0.734225631818182

00:26:23.964 --> 00:26:25.770 recharge sodium ions towards it,

NOTE Confidence: 0.734225631818182

00:26:25.770 --> 00:26:29.922 we can separate these two sodium

NOTE Confidence: 0.734225631818182

00:26:29.922 --> 00:26:30.614 compartments.

NOTE Confidence: 0.788664675555556

00:26:30.620 --> 00:26:32.671 And this is a theory which we've

NOTE Confidence: 0.788664675555556

00:26:32.671 --> 00:26:34.343 contributed to, and a key.

NOTE Confidence: 0.788664675555556

00:26:34.343 --> 00:26:37.506 Two key factors that we point out in in

NOTE Confidence: 0.788664675555556

00:26:37.506 --> 00:26:39.568 this theoretical and practical demonstration

NOTE Confidence: 0.788664675555556

00:26:39.568 --> 00:26:43.010 of pages like this is the fact that.

NOTE Confidence: 0.788664675555556

00:26:43.010 --> 00:26:45.610 There is a certain bound fraction of sodium

NOTE Confidence: 0.788664675555556

00:26:45.610 --> 00:26:47.688 towards these agents that's important,

NOTE Confidence: 0.788664675555556

00:26:47.690 --> 00:26:50.938 but also their exchange and these two

NOTE Confidence: 0.788664675555556

00:26:50.938 --> 00:26:53.811 mechanisms have NKX actually contribute to

NOTE Confidence: 0.788664675555556

00:26:53.811 --> 00:26:57.800 how much the sodium signal will be shifted.

NOTE Confidence: 0.788664675555556

00:26:57.800 --> 00:26:59.700 So the shift ability factor,

NOTE Confidence: 0.788664675555556

00:26:59.700 --> 00:27:02.916 but also how these signals could be broadened

NOTE Confidence: 0.788664675555556

00:27:02.916 --> 00:27:05.670 because of their kind of like nature.

NOTE Confidence: 0.788664675555556

00:27:05.670 --> 00:27:08.294 So, uh, another key thing that we point
NOTE Confidence: 0.7886646755555556

00:27:08.294 --> 00:27:10.562 out is that these shifted signals
NOTE Confidence: 0.7886646755555556

00:27:10.562 --> 00:27:13.329 brought in signals of of of sodium
NOTE Confidence: 0.7886646755555556

00:27:13.329 --> 00:27:15.812 that we will observe is dependent
NOTE Confidence: 0.7886646755555556

00:27:15.812 --> 00:27:18.570 on the sodium concentration on the
NOTE Confidence: 0.7886646755555556

00:27:18.570 --> 00:27:20.310 on the agent concentration.
NOTE Confidence: 0.7886646755555556

00:27:20.310 --> 00:27:22.750 And here we are limited by the fact
NOTE Confidence: 0.7886646755555556

00:27:22.750 --> 00:27:25.232 that we need sufficient amount of
NOTE Confidence: 0.7886646755555556

00:27:25.232 --> 00:27:27.920 this agent present to process certain
NOTE Confidence: 0.7886646755555556

00:27:27.993 --> 00:27:30.268 for the broadening and therefore
NOTE Confidence: 0.7886646755555556

00:27:30.270 --> 00:27:33.476 this is something that will act as
NOTE Confidence: 0.7886646755555556

00:27:33.476 --> 00:27:35.609 a benefit for certain sensor.
NOTE Confidence: 0.7886646755555556

00:27:35.609 --> 00:27:38.027 But it was not necessary for
NOTE Confidence: 0.7886646755555556

00:27:38.027 --> 00:27:40.179 them for the poor concepts.
NOTE Confidence: 0.7886646755555556

00:27:40.180 --> 00:27:42.430 So our expected idea for these
NOTE Confidence: 0.7886646755555556

00:27:42.430 --> 00:27:44.516 experimentation is that before we add

NOTE Confidence: 0.788664675555556
00:27:44.516 --> 00:27:46.240 the agent, we're seeing one single,
NOTE Confidence: 0.788664675555556
00:27:46.240 --> 00:27:48.040 and after we add this agent,
NOTE Confidence: 0.788664675555556
00:27:48.040 --> 00:27:49.880 we're gonna separate the signal.
NOTE Confidence: 0.788664675555556
00:27:49.880 --> 00:27:52.624 Now you see three and I point out
NOTE Confidence: 0.788664675555556
00:27:52.624 --> 00:27:54.918 three because you also have sodium.
NOTE Confidence: 0.788664675555556
00:27:54.920 --> 00:27:56.942 Plenty of sodium also in the
NOTE Confidence: 0.788664675555556
00:27:56.942 --> 00:27:57.616 blood department.
NOTE Confidence: 0.788664675555556
00:27:57.620 --> 00:28:00.548 But because the the blood department is much
NOTE Confidence: 0.788664675555556
00:28:00.548 --> 00:28:03.219 smaller than the interstitial compartment,
NOTE Confidence: 0.788664675555556
00:28:03.220 --> 00:28:05.494 these representative amplitudes
NOTE Confidence: 0.788664675555556
00:28:05.494 --> 00:28:08.634 of these beats are depicted.
NOTE Confidence: 0.788664675555556
00:28:08.634 --> 00:28:11.658 So in vivo inside a tumor voxel.
NOTE Confidence: 0.788664675555556
00:28:11.660 --> 00:28:13.240 This is what we see.
NOTE Confidence: 0.788664675555556
00:28:13.240 --> 00:28:15.030 This is before the agent.
NOTE Confidence: 0.788664675555556
00:28:15.030 --> 00:28:16.730 It's been separated here.
NOTE Confidence: 0.788664675555556

00:28:16.730 --> 00:28:18.855 And outside of the tumor,
NOTE Confidence: 0.788664675555556

00:28:18.860 --> 00:28:20.948 we see something that's similar but
NOTE Confidence: 0.788664675555556

00:28:20.948 --> 00:28:23.370 to the shifting and the broadening
NOTE Confidence: 0.788664675555556

00:28:23.370 --> 00:28:25.440 is to some lesser extent.
NOTE Confidence: 0.788664675555556

00:28:25.440 --> 00:28:27.316 So this is kind of what we
NOTE Confidence: 0.788664675555556

00:28:27.316 --> 00:28:28.120 typically do nowadays,
NOTE Confidence: 0.788664675555556

00:28:28.120 --> 00:28:30.088 and this is work by Mohammad Khan who
NOTE Confidence: 0.788664675555556

00:28:30.088 --> 00:28:32.179 did his thesis work on this project.
NOTE Confidence: 0.788664675555556

00:28:32.180 --> 00:28:34.088 Is is this is the conventional
NOTE Confidence: 0.788664675555556

00:28:34.088 --> 00:28:35.360 location of the tumor.
NOTE Confidence: 0.788664675555556

00:28:35.360 --> 00:28:36.945 We inject the agent to
NOTE Confidence: 0.788664675555556

00:28:36.945 --> 00:28:38.213 identify the blood compartment,
NOTE Confidence: 0.788664675555556

00:28:38.220 --> 00:28:39.544 interstitial compartment,
NOTE Confidence: 0.788664675555556

00:28:39.544 --> 00:28:41.530 interstitial intracellular compartment
NOTE Confidence: 0.788664675555556

00:28:41.530 --> 00:28:44.178 in terms of sodium.
NOTE Confidence: 0.788664675555556

00:28:44.180 --> 00:28:45.800 We integrate these signals to

NOTE Confidence: 0.788664675555556
00:28:45.800 --> 00:28:47.096 get maps like this,
NOTE Confidence: 0.788664675555556
00:28:47.100 --> 00:28:48.920 and using a combination of these two,
NOTE Confidence: 0.788664675555556
00:28:48.920 --> 00:28:50.680 we can get what's called
NOTE Confidence: 0.788664675555556
00:28:50.680 --> 00:28:51.736 an endothelial gradient.
NOTE Confidence: 0.788664675555556
00:28:51.740 --> 00:28:53.655 This is asserting gradient representing
NOTE Confidence: 0.788664675555556
00:28:53.655 --> 00:28:55.570 the and the feeling department.
NOTE Confidence: 0.788664675555556
00:28:55.570 --> 00:28:57.100 And this is the critical one
NOTE Confidence: 0.788664675555556
00:28:57.100 --> 00:28:58.510 that we will talk about,
NOTE Confidence: 0.788664675555556
00:28:58.510 --> 00:29:00.725 which is the transmembrane gradient
NOTE Confidence: 0.788664675555556
00:29:00.725 --> 00:29:03.588 which is obtained from the intracellular
NOTE Confidence: 0.788664675555556
00:29:03.588 --> 00:29:06.448 and the interstitial signals also.
NOTE Confidence: 0.788664675555556
00:29:06.450 --> 00:29:08.952 And we we can now map this into ID
NOTE Confidence: 0.788664675555556
00:29:08.952 --> 00:29:11.239 to get the transmembrane gradient
NOTE Confidence: 0.788664675555556
00:29:11.239 --> 00:29:13.863 how it appears within the tumor.
NOTE Confidence: 0.788664675555556
00:29:13.863 --> 00:29:17.261 I point out there's these blobs of high
NOTE Confidence: 0.788664675555556

00:29:17.261 --> 00:29:20.146 intense signal represents the ventricles.
NOTE Confidence: 0.788664675555556

00:29:20.150 --> 00:29:22.050 Ventricles hasn't has a
NOTE Confidence: 0.788664675555556

00:29:22.050 --> 00:29:24.425 lot of sodium in them,
NOTE Confidence: 0.788664675555556

00:29:24.430 --> 00:29:28.315 and that has variety of them applications.
NOTE Confidence: 0.788664675555556

00:29:28.320 --> 00:29:31.200 Or other disease disorders as well,
NOTE Confidence: 0.788664675555556

00:29:31.200 --> 00:29:33.448 but the key thing is that we can
NOTE Confidence: 0.788664675555556

00:29:33.448 --> 00:29:35.918 obtain a clear readout of the
NOTE Confidence: 0.788664675555556

00:29:35.918 --> 00:29:38.213 transmembrane gradient shown for two
NOTE Confidence: 0.788664675555556

00:29:38.213 --> 00:29:40.028 different three different tumor types,
NOTE Confidence: 0.788664675555556

00:29:40.028 --> 00:29:42.896 and so this is a pretty uniform and
NOTE Confidence: 0.788664675555556

00:29:42.896 --> 00:29:45.619 vigorous observation that we can now make.
NOTE Confidence: 0.788664675555556

00:29:45.620 --> 00:29:48.044 We even began to employ these
NOTE Confidence: 0.788664675555556

00:29:48.044 --> 00:29:49.660 methods for variety of
NOTE Confidence: 0.565210293181818

00:29:49.740 --> 00:29:51.070 different treatments.
NOTE Confidence: 0.88799386

00:29:53.140 --> 00:29:56.940 And and so this is a very unique entry.
NOTE Confidence: 0.88799386

00:29:56.940 --> 00:29:58.571 Genic antiangiogenic treatment and

NOTE Confidence: 0.88799386

00:29:58.571 --> 00:30:01.420 what is shown here is a comparison

NOTE Confidence: 0.88799386

00:30:01.485 --> 00:30:03.900 of what's your afternoon, does it?

NOTE Confidence: 0.88799386

00:30:03.900 --> 00:30:05.500 It it blunts it.

NOTE Confidence: 0.88799386

00:30:05.500 --> 00:30:08.028 It sort of impedes that's in the growth

NOTE Confidence: 0.88799386

00:30:08.028 --> 00:30:10.969 which is most significant within two weeks.

NOTE Confidence: 0.88799386

00:30:10.970 --> 00:30:12.972 And this kind of effect can be

NOTE Confidence: 0.88799386

00:30:12.972 --> 00:30:15.605 read out by the teenage as well

NOTE Confidence: 0.88799386

00:30:15.605 --> 00:30:17.309 as the transmembrane gradient.

NOTE Confidence: 0.88799386

00:30:17.310 --> 00:30:20.187 As you can see the sorafenib against

NOTE Confidence: 0.88799386

00:30:20.187 --> 00:30:24.340 renormalize the pH with treatment and.

NOTE Confidence: 0.88799386

00:30:24.340 --> 00:30:27.526 As well as normal, you know.

NOTE Confidence: 0.88799386

00:30:27.530 --> 00:30:29.734 Strengthening the sodium transmembrane

NOTE Confidence: 0.88799386

00:30:29.734 --> 00:30:31.938 gradient upon treatment even

NOTE Confidence: 0.88799386

00:30:31.938 --> 00:30:34.253 the Chamber making it similar

NOTE Confidence: 0.88799386

00:30:34.253 --> 00:30:36.448 to the normal tissue as well,

NOTE Confidence: 0.88799386

00:30:36.448 --> 00:30:39.160 so I hope that's been able to show
NOTE Confidence: 0.88799386

00:30:39.241 --> 00:30:41.162 within the last few minutes is
NOTE Confidence: 0.88799386

00:30:41.162 --> 00:30:43.654 that we now have a quote which can
NOTE Confidence: 0.88799386

00:30:43.654 --> 00:30:45.826 sense both quote photon and sodium.
NOTE Confidence: 0.88799386

00:30:45.830 --> 00:30:49.178 A lot of credit to both.
NOTE Confidence: 0.88799386

00:30:49.180 --> 00:30:51.890 I'm sharing design quotes of
NOTE Confidence: 0.88799386

00:30:51.890 --> 00:30:53.516 this particular quote,
NOTE Confidence: 0.88799386

00:30:53.520 --> 00:30:54.924 and quotes like this,
NOTE Confidence: 0.88799386

00:30:54.924 --> 00:30:57.849 which with proton imaging can be a very
NOTE Confidence: 0.88799386

00:30:57.849 --> 00:31:00.519 powerful proton sensor for pH imaging,
NOTE Confidence: 0.88799386

00:31:00.519 --> 00:31:03.678 but also a sodium sensor in terms
NOTE Confidence: 0.88799386

00:31:03.678 --> 00:31:05.148 of its its signal shifted.
NOTE Confidence: 0.679780554285714

00:31:07.400 --> 00:31:10.515 It it can be also used simultaneously.
NOTE Confidence: 0.679780554285714

00:31:10.520 --> 00:31:12.008 So I hope I've what I've
NOTE Confidence: 0.679780554285714

00:31:12.008 --> 00:31:13.420 shown is that all cells,
NOTE Confidence: 0.679780554285714

00:31:13.420 --> 00:31:16.396 not just excitable neurons and muscle,

NOTE Confidence: 0.679780554285714

00:31:16.400 --> 00:31:18.715 generate and receive by electrical

NOTE Confidence: 0.679780554285714

00:31:18.715 --> 00:31:21.169 signals that are encoded.

NOTE Confidence: 0.679780554285714

00:31:21.170 --> 00:31:24.135 Within changes in the transmembrane

NOTE Confidence: 0.679780554285714

00:31:24.135 --> 00:31:26.360 potential and the iron fluxes that

NOTE Confidence: 0.679780554285714

00:31:26.360 --> 00:31:28.426 occur at the cell membrane and

NOTE Confidence: 0.679780554285714

00:31:28.426 --> 00:31:29.872 these things happen regularly,

NOTE Confidence: 0.679780554285714

00:31:29.872 --> 00:31:31.924 you know on timescales of milliseconds,

NOTE Confidence: 0.679780554285714

00:31:31.930 --> 00:31:34.270 seconds to even days.

NOTE Confidence: 0.679780554285714

00:31:34.270 --> 00:31:36.610 But these are inextricably

NOTE Confidence: 0.679780554285714

00:31:36.610 --> 00:31:38.940 regulated by catabolism,

NOTE Confidence: 0.679780554285714

00:31:38.940 --> 00:31:44.318 and that is the connection that it is.

NOTE Confidence: 0.679780554285714

00:31:44.320 --> 00:31:48.128 This is needed to find the proper readouts

NOTE Confidence: 0.679780554285714

00:31:48.128 --> 00:31:51.237 of various treatments that we see.

NOTE Confidence: 0.679780554285714

00:31:51.240 --> 00:31:53.544 And I, I think this is another way of

NOTE Confidence: 0.679780554285714

00:31:53.544 --> 00:31:55.820 saying this is that we need advancing

NOTE Confidence: 0.679780554285714

00:31:55.820 --> 00:31:57.827 before imaging methods to assess the
NOTE Confidence: 0.679780554285714

00:31:57.827 --> 00:32:00.206 non genetic by physical aspects of
NOTE Confidence: 0.679780554285714

00:32:00.206 --> 00:32:01.942 tumor microenvironment that regulates
NOTE Confidence: 0.679780554285714

00:32:01.942 --> 00:32:03.610 balance between normal growth
NOTE Confidence: 0.679780554285714

00:32:03.610 --> 00:32:06.245 but also the disorganization that
NOTE Confidence: 0.679780554285714

00:32:06.245 --> 00:32:10.800 happened with most solid solid cancer.
NOTE Confidence: 0.679780554285714

00:32:10.800 --> 00:32:12.250 But importantly,
NOTE Confidence: 0.679780554285714

00:32:12.250 --> 00:32:15.150 simultaneous imaging invasion and
NOTE Confidence: 0.679780554285714

00:32:15.150 --> 00:32:18.250 qualification can hold a promise for
NOTE Confidence: 0.679780554285714

00:32:18.250 --> 00:32:20.620 early cancer diagnosis and tracking
NOTE Confidence: 0.679780554285714

00:32:20.711 --> 00:32:24.978 therapies. From chemotherapy to two.
NOTE Confidence: 0.679780554285714

00:32:24.980 --> 00:32:26.668 There's always grateful for
NOTE Confidence: 0.679780554285714

00:32:26.668 --> 00:32:29.200 tonight support and this work is
NOTE Confidence: 0.679780554285714

00:32:29.277 --> 00:32:31.457 unique collaboration among many
NOTE Confidence: 0.679780554285714

00:32:31.460 --> 00:32:34.760 colleagues within our group.
NOTE Confidence: 0.679780554285714

00:32:34.760 --> 00:32:38.040 Khan and John Walsh,

NOTE Confidence: 0.679780554285714
00:32:38.040 --> 00:32:38.826 PhD and MD,
NOTE Confidence: 0.679780554285714
00:32:38.826 --> 00:32:40.398 PhD students are involved in a
NOTE Confidence: 0.679780554285714
00:32:40.398 --> 00:32:41.460 lot of this work,
NOTE Confidence: 0.679780554285714
00:32:41.460 --> 00:32:43.135 but also by colleagues in
NOTE Confidence: 0.679780554285714
00:32:43.135 --> 00:32:44.475 terms of post starts.
NOTE Confidence: 0.679780554285714
00:32:44.480 --> 00:32:45.880 You're still present Doctor
NOTE Confidence: 0.679780554285714
00:32:45.880 --> 00:32:47.980 Kumar Mishra and and the high
NOTE Confidence: 0.679780554285714
00:32:48.044 --> 00:32:50.009 leverage but also my colleagues.
NOTE Confidence: 0.599430574285714
00:32:52.120 --> 00:32:54.205 Within radiology and
NOTE Confidence: 0.599430574285714
00:32:54.205 --> 00:32:56.985 surgery that department so.
NOTE Confidence: 0.599430574285714
00:32:56.990 --> 00:33:00.770 And I thank you for your.
NOTE Confidence: 0.599430574285714
00:33:00.770 --> 00:33:01.340 Your attention.
NOTE Confidence: 0.753175349
00:33:02.520 --> 00:33:04.820 Thanks, thanks very much it.
NOTE Confidence: 0.753175349
00:33:04.820 --> 00:33:06.480 I think that was great.
NOTE Confidence: 0.753175349
00:33:06.480 --> 00:33:08.560 You mentioned chemotherapy and
NOTE Confidence: 0.753175349

00:33:08.560 --> 00:33:10.013 immunotherapy, and you know,
NOTE Confidence: 0.753175349

00:33:10.013 --> 00:33:12.190 our next talk is from a radiation
NOTE Confidence: 0.753175349

00:33:12.258 --> 00:33:14.796 oncologist and one wonders whether this
NOTE Confidence: 0.753175349

00:33:14.796 --> 00:33:17.425 might also help identify tumors and
NOTE Confidence: 0.753175349

00:33:17.425 --> 00:33:20.215 tract tumors that are being irradiated.
NOTE Confidence: 0.753175349

00:33:20.220 --> 00:33:23.220 Since, as he well knows,
NOTE Confidence: 0.753175349

00:33:23.220 --> 00:33:25.638 it is that his doctor Hanson.
NOTE Confidence: 0.753175349

00:33:25.640 --> 00:33:26.908 It is sometimes confusing
NOTE Confidence: 0.753175349

00:33:26.908 --> 00:33:28.176 after someone's been treated,
NOTE Confidence: 0.753175349

00:33:28.180 --> 00:33:31.474 whether there's active tumor or or not.
NOTE Confidence: 0.753175349

00:33:31.474 --> 00:33:33.330 So without further ado.
NOTE Confidence: 0.753175349

00:33:33.330 --> 00:33:35.880 Guy James Hansen is an associate
NOTE Confidence: 0.753175349

00:33:35.880 --> 00:33:37.580 professor of therapeutic radiology
NOTE Confidence: 0.753175349

00:33:37.651 --> 00:33:40.009 and chief of the Gamma Knife
NOTE Confidence: 0.753175349

00:33:40.009 --> 00:33:41.581 program in therapeutic radiology.
NOTE Confidence: 0.753175349

00:33:41.590 --> 00:33:43.780 He received his medical degree

NOTE Confidence: 0.753175349

00:33:43.780 --> 00:33:46.522 from UCLA School of Medicine and

NOTE Confidence: 0.753175349

00:33:46.522 --> 00:33:48.897 Masters degree in biochemistry and

NOTE Confidence: 0.753175349

00:33:48.897 --> 00:33:51.470 Molecular Biology at UCLA as well.

NOTE Confidence: 0.753175349

00:33:51.470 --> 00:33:52.192 Doctor Hanson,

NOTE Confidence: 0.753175349

00:33:52.192 --> 00:33:54.358 Clinical area of expertise is gamma

NOTE Confidence: 0.753175349

00:33:54.358 --> 00:33:56.065 knife stereotactic radiosurgery for the

NOTE Confidence: 0.753175349

00:33:56.065 --> 00:33:58.228 premium of CNS tumors had neck tumors,

NOTE Confidence: 0.753175349

00:33:58.230 --> 00:34:00.330 lung cancer as well as lymphoma,

NOTE Confidence: 0.753175349

00:34:00.330 --> 00:34:00.604 skin,

NOTE Confidence: 0.753175349

00:34:00.604 --> 00:34:03.070 GI and GUI will bet that he spends more

NOTE Confidence: 0.753175349

00:34:03.132 --> 00:34:05.739 time on CNS disease than other things.

NOTE Confidence: 0.753175349

00:34:05.740 --> 00:34:07.948 But he can tell us his research focus

NOTE Confidence: 0.753175349

00:34:07.948 --> 00:34:09.831 is studying the interplay between

NOTE Confidence: 0.753175349

00:34:09.831 --> 00:34:11.523 autoimmunity and malignancy and

NOTE Confidence: 0.753175349

00:34:11.523 --> 00:34:14.058 attempting to harness and optimize select

NOTE Confidence: 0.753175349

00:34:14.058 --> 00:34:16.068 autoantibodies to use against cancer.

NOTE Confidence: 0.753175349

00:34:16.070 --> 00:34:17.642 James, thanks for.

NOTE Confidence: 0.753175349

00:34:17.642 --> 00:34:18.690 Joining us.

NOTE Confidence: 0.93134971625

00:34:19.310 --> 00:34:20.620 Thank you and thank you

NOTE Confidence: 0.93134971625

00:34:20.620 --> 00:34:21.406 for that introduction.

NOTE Confidence: 0.93134971625

00:34:21.410 --> 00:34:23.356 And yes, if if you can explain

NOTE Confidence: 0.93134971625

00:34:23.356 --> 00:34:24.589 my clinical career to me,

NOTE Confidence: 0.93134971625

00:34:24.590 --> 00:34:26.058 that would be great.

NOTE Confidence: 0.93134971625

00:34:26.058 --> 00:34:29.950 I would love to. But it's hot.

NOTE Confidence: 0.93134971625

00:34:29.950 --> 00:34:31.186 Alright, so let's see,

NOTE Confidence: 0.93134971625

00:34:31.186 --> 00:34:33.630 can you see my slides and hear me?

NOTE Confidence: 0.75257992375

00:34:33.640 --> 00:34:35.090 Yeah, it's in that presentation

NOTE Confidence: 0.75257992375

00:34:35.090 --> 00:34:36.250 now that's great. Yeah

NOTE Confidence: 0.95649372

00:34:36.300 --> 00:34:37.724 alright. Here we go.

NOTE Confidence: 0.95649372

00:34:37.724 --> 00:34:40.180 So I'm gonna be talking today about

NOTE Confidence: 0.95649372

00:34:40.180 --> 00:34:42.900 my particular interest in using

NOTE Confidence: 0.95649372

00:34:42.900 --> 00:34:45.076 lupus antibodies against cancer,

NOTE Confidence: 0.95649372

00:34:45.080 --> 00:34:48.370 and in this case, how we can maybe use lupus

NOTE Confidence: 0.95649372

00:34:48.444 --> 00:34:51.360 antibodies against brain tumors and so.

NOTE Confidence: 0.95649372

00:34:51.360 --> 00:34:52.752 Already, I probably have lost half

NOTE Confidence: 0.95649372

00:34:52.752 --> 00:34:54.259 of youth that are just saying,

NOTE Confidence: 0.95649372

00:34:54.260 --> 00:34:55.616 well, that's impossible.

NOTE Confidence: 0.95649372

00:34:55.616 --> 00:34:57.424 Antibodies can't do that.

NOTE Confidence: 0.95649372

00:34:57.430 --> 00:34:58.950 But just give me 20 minutes or so,

NOTE Confidence: 0.95649372

00:34:58.950 --> 00:34:59.918 give me a chance.

NOTE Confidence: 0.95649372

00:34:59.918 --> 00:35:01.370 I I think that there's something

NOTE Confidence: 0.95649372

00:35:01.420 --> 00:35:02.970 here that's worth talking about.

NOTE Confidence: 0.95649372

00:35:02.970 --> 00:35:04.150 Do you have some disclosures?

NOTE Confidence: 0.95649372

00:35:04.150 --> 00:35:05.176 I'm a consultant.

NOTE Confidence: 0.95649372

00:35:05.176 --> 00:35:06.940 I have grants from inventor

NOTE Confidence: 0.95649372

00:35:06.940 --> 00:35:09.280 on a patent licensed by this

NOTE Confidence: 0.95649372

00:35:09.280 --> 00:35:11.050 company called Patrys Limited,
NOTE Confidence: 0.95649372

00:35:11.050 --> 00:35:14.067 who has licensed the DEOXY mab technology.
NOTE Confidence: 0.95649372

00:35:14.070 --> 00:35:17.166 So with that said, let's jump head first in.
NOTE Confidence: 0.95649372

00:35:17.170 --> 00:35:19.165 I don't think there's any
NOTE Confidence: 0.95649372

00:35:19.165 --> 00:35:20.761 secret that antibodies have
NOTE Confidence: 0.95649372

00:35:20.761 --> 00:35:22.110 revolutionized our approaches.
NOTE Confidence: 0.95649372

00:35:22.110 --> 00:35:24.777 In modern day two treatment of cancer.
NOTE Confidence: 0.95649372

00:35:24.780 --> 00:35:26.677 But I think it's important to recognize
NOTE Confidence: 0.95649372

00:35:26.677 --> 00:35:28.650 that all the antibodies that we really
NOTE Confidence: 0.95649372

00:35:28.650 --> 00:35:31.084 rely on in the clinic right now are
NOTE Confidence: 0.95649372

00:35:31.084 --> 00:35:33.340 targeted towards extracellular targets.
NOTE Confidence: 0.95649372

00:35:33.340 --> 00:35:35.945 So things like surface receptors
NOTE Confidence: 0.95649372

00:35:35.945 --> 00:35:38.029 or circulating growth factors.
NOTE Confidence: 0.95649372

00:35:38.030 --> 00:35:39.842 But doggone it seems like there
NOTE Confidence: 0.95649372

00:35:39.842 --> 00:35:41.362 are so many intracellular antigens
NOTE Confidence: 0.95649372

00:35:41.362 --> 00:35:43.175 that if we could just get an

NOTE Confidence: 0.95649372

00:35:43.175 --> 00:35:44.598 antibody in there to engage,

NOTE Confidence: 0.95649372

00:35:44.600 --> 00:35:46.922 we could add an entire new

NOTE Confidence: 0.95649372

00:35:46.922 --> 00:35:48.083 dimension to immunotherapy.

NOTE Confidence: 0.95649372

00:35:48.090 --> 00:35:50.305 But the dogma has always

NOTE Confidence: 0.95649372

00:35:50.305 --> 00:35:52.077 been that that's impossible.

NOTE Confidence: 0.95649372

00:35:52.080 --> 00:35:55.520 Antibodies don't penetrate live cells.

NOTE Confidence: 0.95649372

00:35:55.520 --> 00:35:57.466 Now this is where critics will often

NOTE Confidence: 0.95649372

00:35:57.466 --> 00:35:59.407 interrupt me and say that's not true.

NOTE Confidence: 0.95649372

00:35:59.410 --> 00:36:01.370 We have antibodies that are already in

NOTE Confidence: 0.95649372

00:36:01.370 --> 00:36:03.120 clinical use that are internalized.

NOTE Confidence: 0.95649372

00:36:03.120 --> 00:36:04.095 What about cats?

NOTE Confidence: 0.95649372

00:36:04.095 --> 00:36:06.980 I love the TDM ones and I I would

NOTE Confidence: 0.95649372

00:36:06.980 --> 00:36:08.240 say I say DNA.

NOTE Confidence: 0.95649372

00:36:08.240 --> 00:36:09.698 That's not what I'm talking about.

NOTE Confidence: 0.95649372

00:36:09.700 --> 00:36:12.244 I'm talking about an antibody that can get

NOTE Confidence: 0.95649372

00:36:12.244 --> 00:36:15.098 in and engage its actual native antigen.

NOTE Confidence: 0.95649372

00:36:15.100 --> 00:36:16.584 In these ADC constructs,

NOTE Confidence: 0.95649372

00:36:16.584 --> 00:36:18.439 these antibodies are still looking

NOTE Confidence: 0.95649372

00:36:18.439 --> 00:36:20.222 for surface receptors like her

NOTE Confidence: 0.95649372

00:36:20.222 --> 00:36:22.462 two in this example and then the

NOTE Confidence: 0.95649372

00:36:22.462 --> 00:36:24.226 antibody gets eaten up and destroyed

NOTE Confidence: 0.95649372

00:36:24.226 --> 00:36:26.222 in the endosome and lysosome which

NOTE Confidence: 0.95649372

00:36:26.222 --> 00:36:27.554 is great for this mechanism because

NOTE Confidence: 0.95649372

00:36:27.554 --> 00:36:28.460 that's what we want,

NOTE Confidence: 0.95649372

00:36:28.460 --> 00:36:30.294 we want that drug to be released,

NOTE Confidence: 0.95649372

00:36:30.300 --> 00:36:32.508 but that doesn't utilize the exquisite

NOTE Confidence: 0.95649372

00:36:32.508 --> 00:36:34.605 binding specificity of an antibody

NOTE Confidence: 0.95649372

00:36:34.605 --> 00:36:36.288 against intracellular targets.

NOTE Confidence: 0.95649372

00:36:36.290 --> 00:36:37.844 So I think we need an antibody

NOTE Confidence: 0.95649372

00:36:37.844 --> 00:36:39.865 that can get into cells and not get

NOTE Confidence: 0.95649372

00:36:39.865 --> 00:36:41.571 stuck in those Endo celebs, but.

NOTE Confidence: 0.95649372

00:36:41.571 --> 00:36:44.859 How are we going to do that well?

NOTE Confidence: 0.95649372

00:36:44.860 --> 00:36:46.340 I guess we could try to invent one.

NOTE Confidence: 0.95649372

00:36:46.340 --> 00:36:48.746 We could stick things like cell

NOTE Confidence: 0.95649372

00:36:48.746 --> 00:36:50.350 penetrating peptides onto antibodies

NOTE Confidence: 0.95649372

00:36:50.411 --> 00:36:52.235 like that at peptides and such,

NOTE Confidence: 0.95649372

00:36:52.240 --> 00:36:53.508 and that's been tried,

NOTE Confidence: 0.95649372

00:36:53.508 --> 00:36:55.844 but those tend to still get stuck

NOTE Confidence: 0.95649372

00:36:55.844 --> 00:36:56.939 in the endosomes.

NOTE Confidence: 0.95649372

00:36:56.940 --> 00:36:59.350 I guess we could try gene therapy, but boy,

NOTE Confidence: 0.95649372

00:36:59.350 --> 00:37:00.880 that's got all kinds of challenges.

NOTE Confidence: 0.95649372

00:37:00.880 --> 00:37:04.256 I'm going to leave that to other people.

NOTE Confidence: 0.95649372

00:37:04.260 --> 00:37:06.332 Maybe if we can just find a naturally

NOTE Confidence: 0.95649372

00:37:06.332 --> 00:37:07.366 occurring antibody that penetrates

NOTE Confidence: 0.95649372

00:37:07.366 --> 00:37:09.246 cells and use that as a platform to

NOTE Confidence: 0.95649372

00:37:09.300 --> 00:37:11.148 teach us how to invent these antibodies,

NOTE Confidence: 0.95649372

00:37:11.150 --> 00:37:14.055 that seems the most appealing to me.
NOTE Confidence: 0.95649372

00:37:14.060 --> 00:37:16.860 But anybody have any idea where we're
NOTE Confidence: 0.95649372

00:37:16.860 --> 00:37:20.256 going to find an antibody like that well?
NOTE Confidence: 0.95649372

00:37:20.260 --> 00:37:22.488 How about in lupus?
NOTE Confidence: 0.95649372

00:37:22.488 --> 00:37:24.159 Systemic lupus erythematosus?
NOTE Confidence: 0.95649372

00:37:24.160 --> 00:37:26.620 It is the prototype autoimmune disease.
NOTE Confidence: 0.95649372

00:37:26.620 --> 00:37:28.684 Patients suffer widespread tissue
NOTE Confidence: 0.95649372

00:37:28.684 --> 00:37:30.232 destruction and inflammation
NOTE Confidence: 0.95649372

00:37:30.232 --> 00:37:31.780 as their immune
NOTE Confidence: 0.936914994705882

00:37:31.847 --> 00:37:33.149 systems recognize their
NOTE Confidence: 0.936914994705882

00:37:33.149 --> 00:37:34.885 own cells and tissues.
NOTE Confidence: 0.936914994705882

00:37:34.890 --> 00:37:36.948 And one of the laboratory hallmarks of
NOTE Confidence: 0.936914994705882

00:37:36.948 --> 00:37:39.194 lupus is the presence of circulating
NOTE Confidence: 0.936914994705882

00:37:39.194 --> 00:37:40.934 autoantibodies that are reactive
NOTE Confidence: 0.936914994705882

00:37:40.934 --> 00:37:44.108 against the patient's own DNA.
NOTE Confidence: 0.936914994705882

00:37:44.110 --> 00:37:46.280 Now those antibodies are a big mystery.

NOTE Confidence: 0.936914994705882

00:37:46.280 --> 00:37:48.261 We still don't know exactly how they

NOTE Confidence: 0.936914994705882

00:37:48.261 --> 00:37:49.980 contribute to lupus pathophysiology,

NOTE Confidence: 0.936914994705882

00:37:49.980 --> 00:37:53.004 but remarkably it is now finally

NOTE Confidence: 0.936914994705882

00:37:53.004 --> 00:37:55.018 accepted that a small percentage

NOTE Confidence: 0.936914994705882

00:37:55.018 --> 00:37:57.280 of them actually have the ability

NOTE Confidence: 0.936914994705882

00:37:57.354 --> 00:37:59.439 to cross through membranes and

NOTE Confidence: 0.936914994705882

00:37:59.439 --> 00:38:01.524 penetrate into live cell nuclei.

NOTE Confidence: 0.936914994705882

00:38:01.530 --> 00:38:02.906 Well, hey, so there we have it right.

NOTE Confidence: 0.936914994705882

00:38:02.910 --> 00:38:04.896 We have a source of naturally

NOTE Confidence: 0.936914994705882

00:38:04.896 --> 00:38:06.220 occurring cell penetrating antibodies.

NOTE Confidence: 0.936914994705882

00:38:06.220 --> 00:38:08.002 We can use those for all kinds of therapies,

NOTE Confidence: 0.936914994705882

00:38:08.010 --> 00:38:08.438 right?

NOTE Confidence: 0.936914994705882

00:38:08.438 --> 00:38:10.578 Well, hold on now everybody

NOTE Confidence: 0.936914994705882

00:38:10.578 --> 00:38:12.790 we're talking about Lupus right?

NOTE Confidence: 0.936914994705882

00:38:12.790 --> 00:38:15.163 At last I checked Lupus is still

NOTE Confidence: 0.936914994705882

00:38:15.163 --> 00:38:17.158 in the textbooks as a disease.
NOTE Confidence: 0.936914994705882

00:38:17.160 --> 00:38:17.822 And indeed,
NOTE Confidence: 0.936914994705882

00:38:17.822 --> 00:38:20.139 a lot of these cell penetrating lupus
NOTE Confidence: 0.936914994705882

00:38:20.139 --> 00:38:21.919 autoantibodies are just broadly cytotoxic.
NOTE Confidence: 0.936914994705882

00:38:21.920 --> 00:38:23.630 And there there wouldn't be any
NOTE Confidence: 0.936914994705882

00:38:23.630 --> 00:38:25.508 benefit to giving them to a patient.
NOTE Confidence: 0.936914994705882

00:38:25.510 --> 00:38:26.158 But thankfully,
NOTE Confidence: 0.936914994705882

00:38:26.158 --> 00:38:28.426 that's not true for all of them.
NOTE Confidence: 0.936914994705882

00:38:28.430 --> 00:38:30.690 There's an antibody called 310,
NOTE Confidence: 0.936914994705882

00:38:30.690 --> 00:38:32.846 which is the hero of this story.
NOTE Confidence: 0.936914994705882

00:38:32.850 --> 00:38:34.392 It was discovered in the early
NOTE Confidence: 0.936914994705882

00:38:34.392 --> 00:38:36.157 1990s at UCLA by Richard Weisbart
NOTE Confidence: 0.936914994705882

00:38:36.157 --> 00:38:38.203 who's pictured there at the left,
NOTE Confidence: 0.936914994705882

00:38:38.210 --> 00:38:40.156 along with his technician Grace Chan and
NOTE Confidence: 0.936914994705882

00:38:40.156 --> 00:38:41.829 his great colleague Robert Nishimura.
NOTE Confidence: 0.936914994705882

00:38:41.830 --> 00:38:42.852 Their great,

NOTE Confidence: 0.936914994705882
00:38:42.852 --> 00:38:44.896 great friends and colleagues.
NOTE Confidence: 0.936914994705882
00:38:44.900 --> 00:38:47.609 What makes 310 so remarkable is that
NOTE Confidence: 0.936914994705882
00:38:47.609 --> 00:38:50.269 it was isolated from a lupus mouse.
NOTE Confidence: 0.936914994705882
00:38:50.270 --> 00:38:51.914 It penetrates extremely effectively
NOTE Confidence: 0.936914994705882
00:38:51.914 --> 00:38:54.780 specifically into the nucleus of live cells,
NOTE Confidence: 0.936914994705882
00:38:54.780 --> 00:38:56.860 and so it does not go through endosomes,
NOTE Confidence: 0.936914994705882
00:38:56.860 --> 00:38:59.420 and it does not kill or is not
NOTE Confidence: 0.936914994705882
00:38:59.420 --> 00:39:02.118 toxic in any way to normal cells.
NOTE Confidence: 0.936914994705882
00:39:02.120 --> 00:39:03.740 So now we've got our chance.
NOTE Confidence: 0.936914994705882
00:39:03.740 --> 00:39:06.588 Now we have an opportunity to use a
NOTE Confidence: 0.936914994705882
00:39:06.588 --> 00:39:08.850 platform antibody that penetrates cells.
NOTE Confidence: 0.936914994705882
00:39:08.850 --> 00:39:10.068 And in fact,
NOTE Confidence: 0.936914994705882
00:39:10.068 --> 00:39:12.950 as we dive a little deeper into
NOTE Confidence: 0.936914994705882
00:39:12.950 --> 00:39:15.150 how this antibody really works,
NOTE Confidence: 0.936914994705882
00:39:15.150 --> 00:39:17.418 it turns out this antibody is really
NOTE Confidence: 0.936914994705882

00:39:17.418 --> 00:39:19.189 well situated for targeting things
NOTE Confidence: 0.936914994705882

00:39:19.189 --> 00:39:21.758 like tumors or sites of tissue damage.
NOTE Confidence: 0.936914994705882

00:39:21.760 --> 00:39:24.518 And that is because part of its
NOTE Confidence: 0.936914994705882

00:39:24.518 --> 00:39:26.658 mechanism of penetration is dependent
NOTE Confidence: 0.936914994705882

00:39:26.658 --> 00:39:28.430 on presence of extracellular
NOTE Confidence: 0.936914994705882

00:39:28.430 --> 00:39:30.909 DNA or nucleosides in the area.
NOTE Confidence: 0.936914994705882

00:39:30.910 --> 00:39:32.464 So what we're showing on the left
NOTE Confidence: 0.936914994705882

00:39:32.464 --> 00:39:33.781 here is something we call the
NOTE Confidence: 0.936914994705882

00:39:33.781 --> 00:39:35.181 three E 10 bullseye effect of the.
NOTE Confidence: 0.936914994705882

00:39:35.190 --> 00:39:36.765 The dark stain represents where
NOTE Confidence: 0.936914994705882

00:39:36.765 --> 00:39:38.702 the antibody is, and as you see,
NOTE Confidence: 0.936914994705882

00:39:38.702 --> 00:39:40.190 that dark stain is getting lighter
NOTE Confidence: 0.936914994705882

00:39:40.240 --> 00:39:41.758 and lighter as you get further
NOTE Confidence: 0.936914994705882

00:39:41.758 --> 00:39:42.770 out from the center,
NOTE Confidence: 0.936914994705882

00:39:42.770 --> 00:39:44.040 and that's because there's a
NOTE Confidence: 0.936914994705882

00:39:44.040 --> 00:39:45.710 dead cell there in the middle.

NOTE Confidence: 0.936914994705882

00:39:45.710 --> 00:39:47.432 And it's releasing DNA into its

NOTE Confidence: 0.936914994705882

00:39:47.432 --> 00:39:48.909 surroundings and helping the antibody

NOTE Confidence: 0.936914994705882

00:39:48.909 --> 00:39:50.547 penetrate the live cells that are

NOTE Confidence: 0.936914994705882

00:39:50.547 --> 00:39:52.450 closest to it, but less effective.

NOTE Confidence: 0.936914994705882

00:39:52.450 --> 00:39:54.250 As we get further out.

NOTE Confidence: 0.936914994705882

00:39:54.250 --> 00:39:56.058 And in the middle we showed we can

NOTE Confidence: 0.936914994705882

00:39:56.058 --> 00:39:57.293 reproduce this in the laboratory

NOTE Confidence: 0.936914994705882

00:39:57.293 --> 00:39:59.001 just by adding DNA to the antibody.

NOTE Confidence: 0.936914994705882

00:39:59.010 --> 00:40:01.490 At the bottom we allow the antibody to

NOTE Confidence: 0.936914994705882

00:40:01.490 --> 00:40:03.370 penetrate 100% of the cells in the culture,

NOTE Confidence: 0.936914994705882

00:40:03.370 --> 00:40:05.925 so the DNA has to be there.

NOTE Confidence: 0.936914994705882

00:40:05.930 --> 00:40:07.736 And then if you take this antibody

NOTE Confidence: 0.936914994705882

00:40:07.736 --> 00:40:10.117 to mice and you give it to mice that

NOTE Confidence: 0.936914994705882

00:40:10.117 --> 00:40:11.770 don't have any tumors or damage,

NOTE Confidence: 0.936914994705882

00:40:11.770 --> 00:40:14.212 you don't see the antibody really

NOTE Confidence: 0.936914994705882

00:40:14.212 --> 00:40:15.026 going anywhere.
NOTE Confidence: 0.936914994705882

00:40:15.030 --> 00:40:17.270 But if you give it to a mouse with a
NOTE Confidence: 0.912835737222222

00:40:17.332 --> 00:40:20.068 tumor that is necrotic and is releasing DNA,
NOTE Confidence: 0.912835737222222

00:40:20.070 --> 00:40:21.335 you do see the antibody
NOTE Confidence: 0.912835737222222

00:40:21.335 --> 00:40:22.347 localising to that tumor.
NOTE Confidence: 0.912835737222222

00:40:22.350 --> 00:40:23.617 That's what's shown in the top right.
NOTE Confidence: 0.912835737222222

00:40:23.620 --> 00:40:26.230 The brown stain are the nuclei
NOTE Confidence: 0.912835737222222

00:40:26.230 --> 00:40:27.970 penetrated by this antibody.
NOTE Confidence: 0.912835737222222

00:40:27.970 --> 00:40:29.730 So what on Earth is going on here?
NOTE Confidence: 0.912835737222222

00:40:29.730 --> 00:40:31.585 Why is this antibody using
NOTE Confidence: 0.912835737222222

00:40:31.585 --> 00:40:33.069 DNA to penetrate cells?
NOTE Confidence: 0.912835737222222

00:40:33.070 --> 00:40:34.030 How is it doing that?
NOTE Confidence: 0.912835737222222

00:40:34.030 --> 00:40:35.862 Well, that's a little bit of a longer
NOTE Confidence: 0.912835737222222

00:40:35.862 --> 00:40:37.466 story than we have time for today,
NOTE Confidence: 0.912835737222222

00:40:37.470 --> 00:40:39.710 but just to jump to the punch line,
NOTE Confidence: 0.912835737222222

00:40:39.710 --> 00:40:42.134 it is using a specific nucleoside

NOTE Confidence: 0.912835737222222

00:40:42.134 --> 00:40:44.549 salvage pathway to get into live

NOTE Confidence: 0.912835737222222

00:40:44.549 --> 00:40:46.510 cells that are salvaging DNA and

NOTE Confidence: 0.912835737222222

00:40:46.510 --> 00:40:47.790 nucleosides from their surroundings,

NOTE Confidence: 0.912835737222222

00:40:47.790 --> 00:40:50.764 and that transporter is called ENT two.

NOTE Confidence: 0.912835737222222

00:40:50.764 --> 00:40:53.026 It is my best friend transporter

NOTE Confidence: 0.912835737222222

00:40:53.026 --> 00:40:56.259 in the whole world stands for

NOTE Confidence: 0.912835737222222

00:40:56.259 --> 00:40:58.655 equilibrated Nucleoside transporter 2.

NOTE Confidence: 0.912835737222222

00:40:58.660 --> 00:41:00.940 So in order for 3:10 to cross membranes

NOTE Confidence: 0.912835737222222

00:41:00.940 --> 00:41:02.779 to penetrate into cells and nuclei,

NOTE Confidence: 0.912835737222222

00:41:02.780 --> 00:41:04.736 you have to have two things.

NOTE Confidence: 0.912835737222222

00:41:04.740 --> 00:41:07.829 The cell has to express ENT two and

NOTE Confidence: 0.912835737222222

00:41:07.829 --> 00:41:10.272 there has to be DNA or nucleosides

NOTE Confidence: 0.912835737222222

00:41:10.272 --> 00:41:12.816 around that cell so that the antibody

NOTE Confidence: 0.912835737222222

00:41:12.816 --> 00:41:15.492 can bind to the nucleosides and then

NOTE Confidence: 0.912835737222222

00:41:15.492 --> 00:41:18.364 follow them through ENT 2 into the cell.

NOTE Confidence: 0.912835737222222

00:41:18.370 --> 00:41:20.290 And that's why the antibody likes
NOTE Confidence: 0.912835737222222

00:41:20.290 --> 00:41:21.250 to preferentially accumulate
NOTE Confidence: 0.912835737222222

00:41:21.250 --> 00:41:22.810 in vivo insights of damage,
NOTE Confidence: 0.912835737222222

00:41:22.810 --> 00:41:26.044 like tumors where DNA is being released
NOTE Confidence: 0.912835737222222

00:41:26.050 --> 00:41:28.354 and ENT two is salvaging salvaging
NOTE Confidence: 0.912835737222222

00:41:28.354 --> 00:41:31.228 the DNA and along with it the 3:10.
NOTE Confidence: 0.912835737222222

00:41:31.230 --> 00:41:33.150 Networks for injury sites as well,
NOTE Confidence: 0.912835737222222

00:41:33.150 --> 00:41:35.300 and that's what we've seen
NOTE Confidence: 0.912835737222222

00:41:35.300 --> 00:41:36.590 in multiple studies.
NOTE Confidence: 0.912835737222222

00:41:36.590 --> 00:41:37.314 For example,
NOTE Confidence: 0.912835737222222

00:41:37.314 --> 00:41:39.124 moving from left to right,
NOTE Confidence: 0.912835737222222

00:41:39.130 --> 00:41:41.875 if you take the three E 10 antibody and
NOTE Confidence: 0.912835737222222

00:41:41.875 --> 00:41:44.524 you link it to a heat shock protein.
NOTE Confidence: 0.912835737222222

00:41:44.530 --> 00:41:46.930 And then give it to mice or rats.
NOTE Confidence: 0.912835737222222

00:41:46.930 --> 00:41:48.350 Actually that have had strokes.
NOTE Confidence: 0.912835737222222

00:41:48.350 --> 00:41:50.366 You find the antibody gets the heat

NOTE Confidence: 0.912835737222222

00:41:50.366 --> 00:41:52.778 shock protein into the ischemic brain and

NOTE Confidence: 0.912835737222222

00:41:52.778 --> 00:41:55.418 improves neurologic function and recovery.

NOTE Confidence: 0.912835737222222

00:41:55.420 --> 00:41:57.676 In the middle here we're showing

NOTE Confidence: 0.912835737222222

00:41:57.676 --> 00:41:59.180 heart attacks in rabbits.

NOTE Confidence: 0.912835737222222

00:41:59.180 --> 00:42:00.896 The 3:10 antibody finds the site

NOTE Confidence: 0.912835737222222

00:42:00.896 --> 00:42:02.758 of the heart attack and delivers

NOTE Confidence: 0.912835737222222

00:42:02.758 --> 00:42:04.078 the heat shock protein.

NOTE Confidence: 0.912835737222222

00:42:04.080 --> 00:42:05.240 It works remarkably well.

NOTE Confidence: 0.912835737222222

00:42:05.240 --> 00:42:07.550 And on the right we're looking at tumors.

NOTE Confidence: 0.912835737222222

00:42:07.550 --> 00:42:09.797 You take the antibody and you fuse it to P53.

NOTE Confidence: 0.912835737222222

00:42:09.797 --> 00:42:11.699 That protein from long time ago

NOTE Confidence: 0.912835737222222

00:42:11.699 --> 00:42:13.399 and it absolutely localizes the

NOTE Confidence: 0.912835737222222

00:42:13.399 --> 00:42:15.119 tumors and shuts them down.

NOTE Confidence: 0.912835737222222

00:42:15.120 --> 00:42:18.336 So 310 has great potential as a delivery

NOTE Confidence: 0.912835737222222

00:42:18.336 --> 00:42:21.236 vehicle for tumors or sites of damage,

NOTE Confidence: 0.912835737222222

00:42:21.240 --> 00:42:23.525 and there's now more companies
NOTE Confidence: 0.912835737222222

00:42:23.525 --> 00:42:27.190 looking at this than I can even count.
NOTE Confidence: 0.912835737222222

00:42:27.190 --> 00:42:29.227 But that's not all the antibody does.
NOTE Confidence: 0.912835737222222

00:42:29.230 --> 00:42:30.847 It turns out that it does more.
NOTE Confidence: 0.912835737222222

00:42:30.850 --> 00:42:33.796 It's not just a delivery agent.
NOTE Confidence: 0.912835737222222

00:42:33.800 --> 00:42:35.618 When the antibody penetrates into the
NOTE Confidence: 0.912835737222222

00:42:35.618 --> 00:42:38.110 nucleus of a cell, it will bind DNA.
NOTE Confidence: 0.912835737222222

00:42:38.110 --> 00:42:40.030 But if it has its choice,
NOTE Confidence: 0.912835737222222

00:42:40.030 --> 00:42:41.730 it will preferentially bind
NOTE Confidence: 0.912835737222222

00:42:41.730 --> 00:42:43.430 a DNA that's broken.
NOTE Confidence: 0.912835737222222

00:42:43.430 --> 00:42:44.982 And then it's going to mess around with
NOTE Confidence: 0.912835737222222

00:42:44.982 --> 00:42:46.468 DNA repair so it blocks base excision,
NOTE Confidence: 0.912835737222222

00:42:46.470 --> 00:42:46.955 repair,
NOTE Confidence: 0.912835737222222

00:42:46.955 --> 00:42:49.865 and rad 51 mediated molega's recombination.
NOTE Confidence: 0.912835737222222

00:42:49.870 --> 00:42:52.124 And that means it can make cancer
NOTE Confidence: 0.912835737222222

00:42:52.124 --> 00:42:54.026 cells more sensitive to DNA

NOTE Confidence: 0.912835737222222

00:42:54.026 --> 00:42:55.774 damaging therapy like certain

NOTE Confidence: 0.912835737222222

00:42:55.774 --> 00:42:57.085 chemotherapies and radiation.

NOTE Confidence: 0.912835737222222

00:42:57.090 --> 00:42:58.746 But even more significantly,

NOTE Confidence: 0.912835737222222

00:42:58.746 --> 00:43:02.610 if the cancer cell or the tumor has a

NOTE Confidence: 0.912835737222222

00:43:02.610 --> 00:43:05.136 pre-existing defect in DNA repair due

NOTE Confidence: 0.912835737222222

00:43:05.136 --> 00:43:08.430 to a mutation such as Bracco or P-10 loss.

NOTE Confidence: 0.912835737222222

00:43:08.430 --> 00:43:10.030 The antibody doesn't need radiation.

NOTE Confidence: 0.934912074166667

00:43:10.030 --> 00:43:11.294 It doesn't need chemotherapy.

NOTE Confidence: 0.934912074166667

00:43:11.294 --> 00:43:13.190 It will kill that cancer cell

NOTE Confidence: 0.934912074166667

00:43:13.247 --> 00:43:14.981 by itself by causing persistence

NOTE Confidence: 0.934912074166667

00:43:14.981 --> 00:43:17.066 of DNA double strand breaks,

NOTE Confidence: 0.934912074166667

00:43:17.070 --> 00:43:18.804 but that doesn't happen in normal

NOTE Confidence: 0.934912074166667

00:43:18.804 --> 00:43:20.589 cells that have intact DNA repair,

NOTE Confidence: 0.934912074166667

00:43:20.590 --> 00:43:23.500 so we have a selective toxicity.

NOTE Confidence: 0.934912074166667

00:43:23.500 --> 00:43:27.777 4HR deficient tumor cells with this antibody.

NOTE Confidence: 0.934912074166667

00:43:27.780 --> 00:43:31.540 So we reported that quite a while ago,
NOTE Confidence: 0.934912074166667

00:43:31.540 --> 00:43:33.016 and then we asked the question,
NOTE Confidence: 0.934912074166667

00:43:33.020 --> 00:43:34.088 is it just 310?
NOTE Confidence: 0.934912074166667

00:43:34.088 --> 00:43:35.690 Is this just something magic about
NOTE Confidence: 0.934912074166667

00:43:35.753 --> 00:43:37.356 3:10 or is this true for other
NOTE Confidence: 0.934912074166667

00:43:37.360 --> 00:43:38.503 cell penetrating antibodies?
NOTE Confidence: 0.934912074166667

00:43:38.503 --> 00:43:40.408 And it turns out indeed
NOTE Confidence: 0.934912074166667

00:43:40.408 --> 00:43:42.180 it's not just three ten.
NOTE Confidence: 0.934912074166667

00:43:42.180 --> 00:43:43.572 There are antibodies that
NOTE Confidence: 0.934912074166667

00:43:43.572 --> 00:43:45.660 penetrate cells and cut DNA and
NOTE Confidence: 0.934912074166667

00:43:45.721 --> 00:43:47.426 kill the HR deficient cells.
NOTE Confidence: 0.934912074166667

00:43:47.430 --> 00:43:49.680 So there's a pattern emerging here
NOTE Confidence: 0.934912074166667

00:43:49.680 --> 00:43:51.564 where lupus antibodies some lupus
NOTE Confidence: 0.934912074166667

00:43:51.564 --> 00:43:53.472 anti DNA antibodies seem to be
NOTE Confidence: 0.934912074166667

00:43:53.472 --> 00:43:56.410 toxic to HR deficient cancer cells,
NOTE Confidence: 0.934912074166667

00:43:56.410 --> 00:43:58.466 and so then that led us to start

NOTE Confidence: 0.934912074166667
00:43:58.466 --> 00:43:59.980 asking some questions about.
NOTE Confidence: 0.934912074166667
00:43:59.980 --> 00:44:01.582 What does this mean for lupus
NOTE Confidence: 0.934912074166667
00:44:01.582 --> 00:44:03.199 and and cancer risk in lupus?
NOTE Confidence: 0.934912074166667
00:44:03.200 --> 00:44:05.500 And I'm not a rheumatologist.
NOTE Confidence: 0.934912074166667
00:44:05.500 --> 00:44:06.668 I did not know,
NOTE Confidence: 0.934912074166667
00:44:06.668 --> 00:44:08.420 but we started reading and looking.
NOTE Confidence: 0.934912074166667
00:44:08.420 --> 00:44:09.614 And overall,
NOTE Confidence: 0.934912074166667
00:44:09.614 --> 00:44:13.196 cancer risk is increased in lupus,
NOTE Confidence: 0.934912074166667
00:44:13.200 --> 00:44:15.340 but it's driven mostly by
NOTE Confidence: 0.934912074166667
00:44:15.340 --> 00:44:16.196 haematological legacy.
NOTE Confidence: 0.934912074166667
00:44:16.200 --> 00:44:18.215 So if you back up and you say, well,
NOTE Confidence: 0.934912074166667
00:44:18.215 --> 00:44:20.420 let's go tumor type by tumor type,
NOTE Confidence: 0.934912074166667
00:44:20.420 --> 00:44:22.598 you get a surprising finding in
NOTE Confidence: 0.934912074166667
00:44:22.598 --> 00:44:24.743 that breast cancer occurs at a
NOTE Confidence: 0.934912074166667
00:44:24.743 --> 00:44:26.609 lower than expected rate in lupus.
NOTE Confidence: 0.934912074166667

00:44:26.610 --> 00:44:28.290 And this has been widely recognized
NOTE Confidence: 0.934912074166667

00:44:28.290 --> 00:44:28.850 for years,
NOTE Confidence: 0.934912074166667

00:44:28.850 --> 00:44:30.370 but no one can figure out exactly why.
NOTE Confidence: 0.934912074166667

00:44:30.370 --> 00:44:33.540 There's no clear associating factor.
NOTE Confidence: 0.934912074166667

00:44:33.540 --> 00:44:34.758 But if you look a little deeper,
NOTE Confidence: 0.934912074166667

00:44:34.760 --> 00:44:36.590 it looks like it's the triple
NOTE Confidence: 0.934912074166667

00:44:36.590 --> 00:44:38.249 negative breast cancer that is
NOTE Confidence: 0.934912074166667

00:44:38.249 --> 00:44:39.789 specifically suppressed in lupus.
NOTE Confidence: 0.934912074166667

00:44:39.790 --> 00:44:41.939 And we do know that triple negative
NOTE Confidence: 0.934912074166667

00:44:41.939 --> 00:44:44.131 breast cancer is associated with the
NOTE Confidence: 0.934912074166667

00:44:44.131 --> 00:44:46.537 brankis phenotypes and the HR deficiency.
NOTE Confidence: 0.934912074166667

00:44:46.540 --> 00:44:48.016 So then we start to think,
NOTE Confidence: 0.934912074166667

00:44:48.020 --> 00:44:49.940 well, if that's true, like why?
NOTE Confidence: 0.934912074166667

00:44:49.940 --> 00:44:51.986 Why aren't lupus patients making these
NOTE Confidence: 0.934912074166667

00:44:51.986 --> 00:44:53.800 triple negative breast cancers as much?
NOTE Confidence: 0.934912074166667

00:44:53.800 --> 00:44:54.062 Well,

NOTE Confidence: 0.934912074166667
00:44:54.062 --> 00:44:55.634 we know about these DNA damaging
NOTE Confidence: 0.934912074166667
00:44:55.634 --> 00:44:56.743 autoantibodies that are killing
NOTE Confidence: 0.934912074166667
00:44:56.743 --> 00:44:57.859 these HR deficient cells.
NOTE Confidence: 0.934912074166667
00:44:57.860 --> 00:44:59.816 Is it possible that lupus anti
NOTE Confidence: 0.934912074166667
00:44:59.816 --> 00:45:01.120 DNA antibodies actually are
NOTE Confidence: 0.934912074166667
00:45:01.182 --> 00:45:03.038 protective against breast cancer?
NOTE Confidence: 0.934912074166667
00:45:03.040 --> 00:45:03.808 And if so,
NOTE Confidence: 0.934912074166667
00:45:03.808 --> 00:45:05.344 maybe we can re engineer them
NOTE Confidence: 0.934912074166667
00:45:05.344 --> 00:45:07.259 and use them to treat triple
NOTE Confidence: 0.934912074166667
00:45:07.259 --> 00:45:08.859 negative breast cancer and so?
NOTE Confidence: 0.934912074166667
00:45:08.860 --> 00:45:09.848 We're excited about this.
NOTE Confidence: 0.934912074166667
00:45:09.848 --> 00:45:12.210 We sent it in as an opinion letter.
NOTE Confidence: 0.934912074166667
00:45:12.210 --> 00:45:13.986 I thought I was extremely clever.
NOTE Confidence: 0.934912074166667
00:45:13.990 --> 00:45:15.260 I was very impressed with
NOTE Confidence: 0.934912074166667
00:45:15.260 --> 00:45:16.530 myself when I called it.
NOTE Confidence: 0.934912074166667

00:45:16.530 --> 00:45:18.306 The lupus butterfly effect,
NOTE Confidence: 0.934912074166667

00:45:18.306 --> 00:45:21.430 because lupus is the symbol of that.
NOTE Confidence: 0.934912074166667

00:45:21.430 --> 00:45:23.886 Sorry, the butterfly is a symbol of lupus.
NOTE Confidence: 0.934912074166667

00:45:23.890 --> 00:45:25.810 The butterfly effect is a symbol of chaos.
NOTE Confidence: 0.934912074166667

00:45:25.810 --> 00:45:27.710 There's chaos and immunology.
NOTE Confidence: 0.934912074166667

00:45:27.710 --> 00:45:29.610 Chaos of using lupus
NOTE Confidence: 0.934912074166667

00:45:29.610 --> 00:45:31.120 antibodies against cancer.
NOTE Confidence: 0.934912074166667

00:45:31.120 --> 00:45:32.408 I thought it was great title and then
NOTE Confidence: 0.934912074166667

00:45:32.408 --> 00:45:33.658 rear said now you haven't proven it.
NOTE Confidence: 0.934912074166667

00:45:33.660 --> 00:45:35.596 You gotta call the theory so it was
NOTE Confidence: 0.934912074166667

00:45:35.596 --> 00:45:37.500 published as the lupus butterfly theory,
NOTE Confidence: 0.934912074166667

00:45:37.500 --> 00:45:38.724 but I will forever want to
NOTE Confidence: 0.934912074166667

00:45:38.724 --> 00:45:40.340 remember it as the lupus butterfly
NOTE Confidence: 0.934912074166667

00:45:40.340 --> 00:45:41.459 effect theory hypothesis.
NOTE Confidence: 0.934912074166667

00:45:41.460 --> 00:45:44.876 Postulate whatever you want to call it.
NOTE Confidence: 0.934912074166667

00:45:44.880 --> 00:45:45.776 But we do need to prove it,

NOTE Confidence: 0.934912074166667
00:45:45.780 --> 00:45:47.616 so we published that in 2016
NOTE Confidence: 0.934912074166667
00:45:47.616 --> 00:45:50.096 and we started asking around.
NOTE Confidence: 0.934912074166667
00:45:50.100 --> 00:45:51.565 Anybody can help us with
NOTE Confidence: 0.934912074166667
00:45:51.565 --> 00:45:53.368 epidemiology 'cause we have no idea
NOTE Confidence: 0.934912074166667
00:45:53.368 --> 00:45:55.054 what we're doing in that regard.
NOTE Confidence: 0.910918758181818
00:45:55.060 --> 00:45:56.590 And it turns out Lupus is
NOTE Confidence: 0.910918758181818
00:45:56.590 --> 00:45:57.780 rare enough that it's a.
NOTE Confidence: 0.910918758181818
00:45:57.780 --> 00:46:00.354 It's a challenge to actually prove
NOTE Confidence: 0.910918758181818
00:46:00.354 --> 00:46:02.070 the association between lupus
NOTE Confidence: 0.910918758181818
00:46:02.146 --> 00:46:04.426 antibodies and breast cancer risk.
NOTE Confidence: 0.910918758181818
00:46:04.430 --> 00:46:05.954 But not an insurmountable one because
NOTE Confidence: 0.910918758181818
00:46:05.954 --> 00:46:07.814 John Hopkins was able to do it and
NOTE Confidence: 0.910918758181818
00:46:07.814 --> 00:46:09.002 they published it just last year.
NOTE Confidence: 0.910918758181818
00:46:09.010 --> 00:46:10.781 So this. Kind of blew my mind
NOTE Confidence: 0.910918758181818
00:46:10.781 --> 00:46:12.913 and I was very exciting to see
NOTE Confidence: 0.910918758181818

00:46:12.913 --> 00:46:15.008 this the Hopkins Lupus cohort.

NOTE Confidence: 0.910918758181818

00:46:15.008 --> 00:46:17.218 They were able to treat.

NOTE Confidence: 0.910918758181818

00:46:17.220 --> 00:46:19.199 Sorry they were able to analyze

NOTE Confidence: 0.910918758181818

00:46:19.199 --> 00:46:20.994 2000 plus lupus patients that

NOTE Confidence: 0.910918758181818

00:46:20.994 --> 00:46:22.799 entered their cohort without a

NOTE Confidence: 0.910918758181818

00:46:22.799 --> 00:46:24.349 cancer diagnosis and then evaluate

NOTE Confidence: 0.910918758181818

00:46:24.349 --> 00:46:26.030 their risk of breast cancer.

NOTE Confidence: 0.898002588461539

00:46:28.070 --> 00:46:29.855 Over the years and they were able

NOTE Confidence: 0.898002588461539

00:46:29.855 --> 00:46:31.570 to associate that with the patients,

NOTE Confidence: 0.898002588461539

00:46:31.570 --> 00:46:33.678 laboratory studies and anti

NOTE Confidence: 0.898002588461539

00:46:33.678 --> 00:46:35.259 DNA antibody profiles.

NOTE Confidence: 0.898002588461539

00:46:35.260 --> 00:46:37.878 And we do see finally proof that

NOTE Confidence: 0.898002588461539

00:46:37.878 --> 00:46:40.699 there is an association between

NOTE Confidence: 0.898002588461539

00:46:40.700 --> 00:46:42.645 anti double stranded DNA antibody

NOTE Confidence: 0.898002588461539

00:46:42.645 --> 00:46:44.590 positivity and that reduction in

NOTE Confidence: 0.898002588461539

00:46:44.649 --> 00:46:46.803 breast cancer risk patients that make

NOTE Confidence: 0.898002588461539

00:46:46.803 --> 00:46:49.057 those anti D antibodies have 45%

NOTE Confidence: 0.898002588461539

00:46:49.057 --> 00:46:52.159 reduction in the breast cancer risk.

NOTE Confidence: 0.898002588461539

00:46:52.160 --> 00:46:54.184 And if you dig even deeper and you

NOTE Confidence: 0.898002588461539

00:46:54.184 --> 00:46:56.286 stratify the patients based on the amount

NOTE Confidence: 0.898002588461539

00:46:56.286 --> 00:46:58.260 of those antibodies they are making,

NOTE Confidence: 0.898002588461539

00:46:58.260 --> 00:47:00.500 the low producers did not have any

NOTE Confidence: 0.898002588461539

00:47:00.500 --> 00:47:02.239 reduction in breast cancer risk.

NOTE Confidence: 0.898002588461539

00:47:02.240 --> 00:47:04.190 But the high producers had

NOTE Confidence: 0.898002588461539

00:47:04.190 --> 00:47:05.788 a 59% reduction in risk,

NOTE Confidence: 0.898002588461539

00:47:05.788 --> 00:47:07.600 so I've I'm taking this as

NOTE Confidence: 0.898002588461539

00:47:07.665 --> 00:47:08.957 backing up my theory.

NOTE Confidence: 0.898002588461539

00:47:08.960 --> 00:47:10.640 I think the lupus butterfly theory can be

NOTE Confidence: 0.898002588461539

00:47:10.640 --> 00:47:12.199 called the lupus butterfly effect now,

NOTE Confidence: 0.898002588461539

00:47:12.200 --> 00:47:13.838 so I might ask for a revision

NOTE Confidence: 0.898002588461539

00:47:13.838 --> 00:47:14.540 to that article.

NOTE Confidence: 0.898002588461539

00:47:14.540 --> 00:47:16.916 Although it's been five years here.

NOTE Confidence: 0.898002588461539

00:47:16.920 --> 00:47:17.624 But regardless,

NOTE Confidence: 0.898002588461539

00:47:17.624 --> 00:47:19.736 it's it seems like we're learning

NOTE Confidence: 0.898002588461539

00:47:19.736 --> 00:47:21.176 something about lupus antibodies

NOTE Confidence: 0.898002588461539

00:47:21.176 --> 00:47:22.876 and at least breast cancer,

NOTE Confidence: 0.898002588461539

00:47:22.880 --> 00:47:24.524 and it gives me more confidence

NOTE Confidence: 0.898002588461539

00:47:24.524 --> 00:47:26.286 in what we're doing and trying

NOTE Confidence: 0.898002588461539

00:47:26.286 --> 00:47:28.070 to reengineer lupus antibodies

NOTE Confidence: 0.898002588461539

00:47:28.070 --> 00:47:30.300 to treat triple negative breast

NOTE Confidence: 0.898002588461539

00:47:30.368 --> 00:47:31.920 cancer and other tumors.

NOTE Confidence: 0.898002588461539

00:47:31.920 --> 00:47:33.440 So what are we doing in that regard?

NOTE Confidence: 0.898002588461539

00:47:33.440 --> 00:47:34.802 Well? Again.

NOTE Confidence: 0.898002588461539

00:47:34.802 --> 00:47:38.888 I remember and I recognize 310,

NOTE Confidence: 0.898002588461539

00:47:38.890 --> 00:47:39.865 although it's technically

NOTE Confidence: 0.898002588461539

00:47:39.865 --> 00:47:41.165 safe in normal cells.

NOTE Confidence: 0.898002588461539

00:47:41.170 --> 00:47:44.397 It's still a lupus anti DNA antibody.

NOTE Confidence: 0.898002588461539
00:47:44.400 --> 00:47:45.816 And you don't want to give
NOTE Confidence: 0.898002588461539
00:47:45.816 --> 00:47:46.760 anybody lupus like symptoms.
NOTE Confidence: 0.898002588461539
00:47:46.760 --> 00:47:48.832 So we gotta rethink this a little
NOTE Confidence: 0.898002588461539
00:47:48.832 --> 00:47:50.563 bit before we start taking
NOTE Confidence: 0.898002588461539
00:47:50.563 --> 00:47:52.115 this to clinical trials.
NOTE Confidence: 0.898002588461539
00:47:52.120 --> 00:47:54.325 The last thing you want is a lupus FC
NOTE Confidence: 0.898002588461539
00:47:54.325 --> 00:47:56.359 region being administered to patients,
NOTE Confidence: 0.898002588461539
00:47:56.360 --> 00:47:58.712 because the FC is going to activate
NOTE Confidence: 0.898002588461539
00:47:58.712 --> 00:48:01.346 compliment and ABC and all kinds of madness.
NOTE Confidence: 0.898002588461539
00:48:01.350 --> 00:48:03.499 But the good news is, 310 does not
NOTE Confidence: 0.898002588461539
00:48:03.499 --> 00:48:05.710 care whether or not it has the FC tail.
NOTE Confidence: 0.898002588461539
00:48:05.710 --> 00:48:08.190 It'll penetrate cells with or without the FC.
NOTE Confidence: 0.898002588461539
00:48:08.190 --> 00:48:10.032 It'll bind DNA and inhibit DNA
NOTE Confidence: 0.898002588461539
00:48:10.032 --> 00:48:11.730 repair with or without the FC.
NOTE Confidence: 0.898002588461539
00:48:11.730 --> 00:48:13.790 So first thing we've done, cut it off.
NOTE Confidence: 0.898002588461539

00:48:13.790 --> 00:48:15.530 There is no more FC tail,
NOTE Confidence: 0.898002588461539

00:48:15.530 --> 00:48:16.626 the danger is gone.
NOTE Confidence: 0.898002588461539

00:48:16.626 --> 00:48:19.011 And that's how we make what we call
NOTE Confidence: 0.898002588461539

00:48:19.011 --> 00:48:20.716 a single chain variable fragment,
NOTE Confidence: 0.898002588461539

00:48:20.720 --> 00:48:21.103 SCFE.
NOTE Confidence: 0.898002588461539

00:48:21.103 --> 00:48:23.018 It's only the variable sequences
NOTE Confidence: 0.898002588461539

00:48:23.018 --> 00:48:25.530 of the light and heavy chains.
NOTE Confidence: 0.898002588461539

00:48:25.530 --> 00:48:27.205 And that's been optimized to
NOTE Confidence: 0.898002588461539

00:48:27.205 --> 00:48:28.880 increase the affinity for DNA.
NOTE Confidence: 0.898002588461539

00:48:28.880 --> 00:48:30.779 And then we stuck a couple of those
NOTE Confidence: 0.898002588461539

00:48:30.779 --> 00:48:32.633 together to make a dye single chain
NOTE Confidence: 0.898002588461539

00:48:32.633 --> 00:48:34.679 fragments to bump up the avidity for DNA.
NOTE Confidence: 0.898002588461539

00:48:34.680 --> 00:48:36.878 And that works really well against HR
NOTE Confidence: 0.898002588461539

00:48:36.878 --> 00:48:38.450 deficient cancer cells and tumors.
NOTE Confidence: 0.898002588461539

00:48:38.450 --> 00:48:40.280 And that's the product that was
NOTE Confidence: 0.898002588461539

00:48:40.280 --> 00:48:41.852 finally licensed by biotech company

NOTE Confidence: 0.898002588461539
00:48:41.852 --> 00:48:43.579 Patriss as we talked about who
NOTE Confidence: 0.898002588461539
00:48:43.579 --> 00:48:45.133 then has helped with funds to
NOTE Confidence: 0.898002588461539
00:48:45.133 --> 00:48:47.112 allow us to humanize and demonize
NOTE Confidence: 0.898002588461539
00:48:47.112 --> 00:48:49.056 and further optimize the CDR's.
NOTE Confidence: 0.898002588461539
00:48:49.056 --> 00:48:50.760 To develop the antibody,
NOTE Confidence: 0.898002588461539
00:48:50.760 --> 00:48:52.872 I would like to now introduce
NOTE Confidence: 0.898002588461539
00:48:52.872 --> 00:48:55.304 named Deoxy Mab one or DX1 deoxy
NOTE Confidence: 0.898002588461539
00:48:55.304 --> 00:48:57.716 mab 'cause DNA mab for antibody.
NOTE Confidence: 0.898002588461539
00:48:57.720 --> 00:48:58.312 Yeah,
NOTE Confidence: 0.898002588461539
00:48:58.312 --> 00:49:00.088 you get it.
NOTE Confidence: 0.898002588461539
00:49:00.090 --> 00:49:03.354 DX1 is well if ENT two is my
NOTE Confidence: 0.898002588461539
00:49:03.354 --> 00:49:05.009 favorite transporter DX one is
NOTE Confidence: 0.898002588461539
00:49:05.010 --> 00:49:06.310 probably my favorite antibody,
NOTE Confidence: 0.898002588461539
00:49:06.310 --> 00:49:08.593 although there is some other ones that
NOTE Confidence: 0.898002588461539
00:49:08.593 --> 00:49:10.504 are kind of catching my attention too.
NOTE Confidence: 0.898002588461539

00:49:10.510 --> 00:49:11.353 It works great,
NOTE Confidence: 0.898002588461539

00:49:11.353 --> 00:49:12.758 penetrates so clearly into the
NOTE Confidence: 0.898002588461539

00:49:12.758 --> 00:49:14.190 nucleus we see triple negative
NOTE Confidence: 0.898002588461539

00:49:14.190 --> 00:49:16.087 breast cancer cells on the left and
NOTE Confidence: 0.900309922857143

00:49:16.145 --> 00:49:18.265 breast cancer brain Mets else on the right.
NOTE Confidence: 0.900309922857143

00:49:18.270 --> 00:49:19.938 It's killing the cells,
NOTE Confidence: 0.900309922857143

00:49:19.938 --> 00:49:21.606 it's sensitizing to radiation,
NOTE Confidence: 0.900309922857143

00:49:21.610 --> 00:49:23.724 but it's still leaving normal cells alone.
NOTE Confidence: 0.900309922857143

00:49:23.730 --> 00:49:25.846 Just what we want and we are
NOTE Confidence: 0.900309922857143

00:49:25.846 --> 00:49:27.486 excited to move this towards
NOTE Confidence: 0.900309922857143

00:49:27.486 --> 00:49:28.470 clinical trial testing.
NOTE Confidence: 0.900309922857143

00:49:28.470 --> 00:49:29.958 But wait a second did I?
NOTE Confidence: 0.900309922857143

00:49:29.960 --> 00:49:31.725 Am I saying something about
NOTE Confidence: 0.900309922857143

00:49:31.725 --> 00:49:33.230 brain Mets cells but?
NOTE Confidence: 0.834734662142857

00:49:35.650 --> 00:49:36.861 Am I arguing that we could maybe
NOTE Confidence: 0.834734662142857

00:49:36.861 --> 00:49:38.170 be using this to treat brain Mets?

NOTE Confidence: 0.834734662142857
00:49:38.170 --> 00:49:39.430 This is an antibody, right?
NOTE Confidence: 0.834734662142857
00:49:39.430 --> 00:49:40.396 I mean this, the story is
NOTE Confidence: 0.834734662142857
00:49:40.396 --> 00:49:41.663 already kind of far fetched, but.
NOTE Confidence: 0.834734662142857
00:49:41.663 --> 00:49:44.007 Brain Mets well, The thing is one of
NOTE Confidence: 0.834734662142857
00:49:44.007 --> 00:49:46.446 the key biologic markers that predict
NOTE Confidence: 0.834734662142857
00:49:46.446 --> 00:49:48.910 sensitivity to our antibody is loss
NOTE Confidence: 0.834734662142857
00:49:48.910 --> 00:49:51.398 of P-10 even more so than bracket for.
NOTE Confidence: 0.834734662142857
00:49:51.400 --> 00:49:52.904 And I know that all the DNA repair
NOTE Confidence: 0.834734662142857
00:49:52.904 --> 00:49:53.790 experts are probably jumping
NOTE Confidence: 0.834734662142857
00:49:53.790 --> 00:49:55.200 up and down right now saying,
NOTE Confidence: 0.834734662142857
00:49:55.200 --> 00:49:58.546 well the P-10 HR link is not
NOTE Confidence: 0.834734662142857
00:49:58.546 --> 00:50:01.048 completely proven and fine, but.
NOTE Confidence: 0.834734662142857
00:50:01.048 --> 00:50:04.088 Cells at a P-10 deficient are
NOTE Confidence: 0.834734662142857
00:50:04.088 --> 00:50:06.306 killed by this antibody and brain.
NOTE Confidence: 0.834734662142857
00:50:06.306 --> 00:50:08.917 Mints often exhibit P-10 loss even when
NOTE Confidence: 0.834734662142857

00:50:08.917 --> 00:50:11.435 the primary tumor is P 10 positive
NOTE Confidence: 0.834734662142857

00:50:11.440 --> 00:50:14.020 and that's either evolution towards
NOTE Confidence: 0.834734662142857

00:50:14.020 --> 00:50:16.600 metastasis or secretion of P-10
NOTE Confidence: 0.834734662142857

00:50:16.686 --> 00:50:19.536 suppressive micro RNAs by astrocytes.
NOTE Confidence: 0.834734662142857

00:50:19.540 --> 00:50:21.311 It's also worth noting P-10 is lost
NOTE Confidence: 0.834734662142857

00:50:21.311 --> 00:50:23.448 an awful lot in primary GBM, so.
NOTE Confidence: 0.834734662142857

00:50:23.448 --> 00:50:27.672 Maybe we've got treatment for GBM as well.
NOTE Confidence: 0.834734662142857

00:50:27.680 --> 00:50:30.200 But I hear what you're saying.
NOTE Confidence: 0.834734662142857

00:50:30.200 --> 00:50:33.525 Brain Mets brain tumors with an antibody.
NOTE Confidence: 0.834734662142857

00:50:33.530 --> 00:50:35.234 I I don't understand what the
NOTE Confidence: 0.834734662142857

00:50:35.234 --> 00:50:36.086 why the skepticism.
NOTE Confidence: 0.834734662142857

00:50:36.090 --> 00:50:36.662 I mean,
NOTE Confidence: 0.834734662142857

00:50:36.662 --> 00:50:38.806 all we need is DNA and nucleosides
NOTE Confidence: 0.834734662142857

00:50:38.806 --> 00:50:41.130 and the E NT 2 transporter right?
NOTE Confidence: 0.834734662142857

00:50:41.130 --> 00:50:43.090 It seems like the antibody should be able
NOTE Confidence: 0.834734662142857

00:50:43.090 --> 00:50:45.430 to get into the brain tumors just fine it.

NOTE Confidence: 0.834734662142857
00:50:45.430 --> 00:50:49.288 Oh oh right.
NOTE Confidence: 0.834734662142857
00:50:49.290 --> 00:50:50.738 The blood brain barrier.
NOTE Confidence: 0.94686102
00:50:52.760 --> 00:50:56.810 I guess that does pose something of an issue.
NOTE Confidence: 0.94686102
00:50:56.810 --> 00:50:58.595 Maybe I should have thought this through
NOTE Confidence: 0.94686102
00:50:58.595 --> 00:51:00.178 before I signed up for this talk.
NOTE Confidence: 0.94686102
00:51:00.180 --> 00:51:03.230 I guess it's too late to back out now though.
NOTE Confidence: 0.94686102
00:51:03.230 --> 00:51:05.981 If we look really closely at the
NOTE Confidence: 0.94686102
00:51:05.981 --> 00:51:08.463 blood brain barrier and we look in
NOTE Confidence: 0.94686102
00:51:08.463 --> 00:51:10.428 at the brain endothelial cells.
NOTE Confidence: 0.94686102
00:51:10.430 --> 00:51:12.594 Whoa, there's my buddy.
NOTE Confidence: 0.94686102
00:51:12.594 --> 00:51:15.153 E and T2. The luminal surface
NOTE Confidence: 0.94686102
00:51:15.153 --> 00:51:16.708 of the brain endothelial cell.
NOTE Confidence: 0.94686102
00:51:16.710 --> 00:51:19.218 And it actually regulates nucleoside flux
NOTE Confidence: 0.94686102
00:51:19.220 --> 00:51:22.036 into and out of the central nervous system.
NOTE Confidence: 0.94686102
00:51:22.040 --> 00:51:23.120 So wait a second.
NOTE Confidence: 0.94686102

00:51:23.120 --> 00:51:25.739 This is all starting to come full circle now.
NOTE Confidence: 0.94686102

00:51:25.740 --> 00:51:27.786 I think I'm arguing that our
NOTE Confidence: 0.94686102

00:51:27.786 --> 00:51:30.269 antibody DX1 can get over the river,
NOTE Confidence: 0.94686102

00:51:30.270 --> 00:51:32.700 the bloodstream, and through the woods.
NOTE Confidence: 0.94686102

00:51:32.700 --> 00:51:34.240 The blood brain barrier and
NOTE Confidence: 0.94686102

00:51:34.240 --> 00:51:35.472 into the brain tumor.
NOTE Confidence: 0.94686102

00:51:35.480 --> 00:51:38.112 We will go where the antibody will
NOTE Confidence: 0.94686102

00:51:38.112 --> 00:51:40.950 then bind DNA and inhibit DNA repair
NOTE Confidence: 0.94686102

00:51:40.950 --> 00:51:43.870 and kill those brain Mets and also.
NOTE Confidence: 0.94686102

00:51:43.870 --> 00:51:46.018 The possibly last owner.
NOTE Confidence: 0.966709268333333

00:51:48.370 --> 00:51:50.706 And we are seeing that this indeed is
NOTE Confidence: 0.966709268333333

00:51:50.706 --> 00:51:55.460 working out very well season. Sorry.
NOTE Confidence: 0.966709268333333

00:51:55.460 --> 00:51:57.788 We are finding that DX1 does cross transwell
NOTE Confidence: 0.966709268333333

00:51:57.788 --> 00:51:59.851 models of the blood brain barrier and it
NOTE Confidence: 0.966709268333333

00:51:59.851 --> 00:52:02.098 does so in an EMT 2 dependent manner.
NOTE Confidence: 0.966709268333333

00:52:02.100 --> 00:52:04.020 If you shut down EMT 2 the antibody

NOTE Confidence: 0.966709268333333
00:52:04.020 --> 00:52:05.998 can't get across in the middle panel.
NOTE Confidence: 0.966709268333333
00:52:06.000 --> 00:52:07.775 Here we're showing mice with
NOTE Confidence: 0.966709268333333
00:52:07.775 --> 00:52:08.840 orthotopic brain tumors.
NOTE Confidence: 0.966709268333333
00:52:08.840 --> 00:52:10.520 GBM in this case.
NOTE Confidence: 0.966709268333333
00:52:10.520 --> 00:52:12.620 And we gave the antibodies.
NOTE Confidence: 0.966709268333333
00:52:12.620 --> 00:52:14.398 We gave the mice antibodies labeled so
NOTE Confidence: 0.966709268333333
00:52:14.398 --> 00:52:16.682 that we can see it on imaging and the
NOTE Confidence: 0.966709268333333
00:52:16.682 --> 00:52:18.628 antibody gets into the brain tumor great.
NOTE Confidence: 0.966709268333333
00:52:18.630 --> 00:52:20.303 But not if we treat the mice
NOTE Confidence: 0.966709268333333
00:52:20.303 --> 00:52:21.650 with an inhibitor of ENT two,
NOTE Confidence: 0.966709268333333
00:52:21.650 --> 00:52:23.126 so you shut down ENT 2,
NOTE Confidence: 0.966709268333333
00:52:23.130 --> 00:52:25.050 the antibody can't get into the brain tumor,
NOTE Confidence: 0.966709268333333
00:52:25.050 --> 00:52:27.378 so it's working like we think.
NOTE Confidence: 0.966709268333333
00:52:27.380 --> 00:52:28.718 And it seems to actually matter.
NOTE Confidence: 0.966709268333333
00:52:28.720 --> 00:52:29.688 It makes a difference.
NOTE Confidence: 0.966709268333333

00:52:29.688 --> 00:52:30.898 The panel on the right.
NOTE Confidence: 0.966709268333333

00:52:30.900 --> 00:52:34.183 These are mice treated with the antibody
NOTE Confidence: 0.966709268333333

00:52:34.183 --> 00:52:37.238 with P-10 deficient patient derived GBM.
NOTE Confidence: 0.966709268333333

00:52:37.240 --> 00:52:38.404 DX1 by itself.
NOTE Confidence: 0.966709268333333

00:52:38.404 --> 00:52:39.180 No radiation.
NOTE Confidence: 0.966709268333333

00:52:39.180 --> 00:52:40.792 No chemotherapy significantly suppresses
NOTE Confidence: 0.966709268333333

00:52:40.792 --> 00:52:43.210 the tumor growth and extends survival.
NOTE Confidence: 0.95907728

00:52:48.680 --> 00:52:51.720 There we go. Brain Mets are a little
NOTE Confidence: 0.95907728

00:52:51.720 --> 00:52:54.234 harder to study, and GBM in mice.
NOTE Confidence: 0.95907728

00:52:54.234 --> 00:52:56.539 Just implant the tumor intracranially
NOTE Confidence: 0.95907728

00:52:56.539 --> 00:52:59.183 and watch and it goes, but that's not
NOTE Confidence: 0.95907728

00:52:59.183 --> 00:53:00.730 really fair for a brain met model.
NOTE Confidence: 0.95907728

00:53:00.730 --> 00:53:03.232 So the way we study brain Mets has been
NOTE Confidence: 0.95907728

00:53:03.232 --> 00:53:05.783 taught to us by our good friend and
NOTE Confidence: 0.95907728

00:53:05.783 --> 00:53:07.915 colleague Jangling Zhao and mastered by
NOTE Confidence: 0.95907728

00:53:07.915 --> 00:53:10.285 research associate my lab benedet caffari.

NOTE Confidence: 0.95907728

00:53:10.290 --> 00:53:14.000 These are not easy experiments.

NOTE Confidence: 0.95907728

00:53:14.000 --> 00:53:15.370 Breast cancer cells are injected

NOTE Confidence: 0.95907728

00:53:15.370 --> 00:53:17.674 into the hearts of the mice to allow

NOTE Confidence: 0.95907728

00:53:17.674 --> 00:53:19.139 them exposure to the circulation,

NOTE Confidence: 0.95907728

00:53:19.140 --> 00:53:21.417 and we use a brain seeking some type of

NOTE Confidence: 0.95907728

00:53:21.417 --> 00:53:23.668 the cancer cells to go to the brains.

NOTE Confidence: 0.95907728

00:53:23.670 --> 00:53:25.917 And you can then track those based

NOTE Confidence: 0.95907728

00:53:25.917 --> 00:53:28.110 on their signal on serial imaging.

NOTE Confidence: 0.95907728

00:53:28.110 --> 00:53:29.964 So if we give the mice brain mats and

NOTE Confidence: 0.95907728

00:53:29.964 --> 00:53:32.089 we treat them with tail vein injections

NOTE Confidence: 0.95907728

00:53:32.090 --> 00:53:34.030 with control, or the antibody,

NOTE Confidence: 0.95907728

00:53:34.030 --> 00:53:35.880 just the antibody, no radiation,

NOTE Confidence: 0.95907728

00:53:35.880 --> 00:53:36.578 no chemotherapy.

NOTE Confidence: 0.95907728

00:53:36.578 --> 00:53:39.021 I think that picture up in the

NOTE Confidence: 0.95907728

00:53:39.021 --> 00:53:40.670 top right says it all.

NOTE Confidence: 0.95907728

00:53:40.670 --> 00:53:42.094 It suppresses the brain
NOTE Confidence: 0.95907728

00:53:42.094 --> 00:53:43.634 Mets quite phenomenally,
NOTE Confidence: 0.95907728

00:53:43.634 --> 00:53:47.186 and it does also extend survival,
NOTE Confidence: 0.95907728

00:53:47.190 --> 00:53:48.550 so this is looking really, really good.
NOTE Confidence: 0.95907728

00:53:48.550 --> 00:53:50.470 But now I start to hear the words
NOTE Confidence: 0.95907728

00:53:50.531 --> 00:53:52.050 again in the back of my head.
NOTE Confidence: 0.95907728

00:53:52.050 --> 00:53:54.462 I don't know if anybody else can hear them.
NOTE Confidence: 0.95907728

00:53:54.470 --> 00:53:55.640 Do we really need a new
NOTE Confidence: 0.95907728

00:53:55.640 --> 00:53:56.790 way to treat breast cancer?
NOTE Confidence: 0.95907728

00:53:56.790 --> 00:53:58.014 Brain Mets, I think isn't that
NOTE Confidence: 0.95907728

00:53:58.014 --> 00:53:59.150 what the gamma knife is for?
NOTE Confidence: 0.95907728

00:53:59.150 --> 00:53:59.910 It's it's easy, right?
NOTE Confidence: 0.95907728

00:53:59.910 --> 00:54:00.670 You see a brain,
NOTE Confidence: 0.95907728

00:54:00.670 --> 00:54:02.480 but you just send the patient to the
NOTE Confidence: 0.95907728

00:54:02.480 --> 00:54:04.642 gamma knife and I would say, Oh no.
NOTE Confidence: 0.95907728

00:54:04.642 --> 00:54:06.266 It's not so easy.

NOTE Confidence: 0.95907728

00:54:06.270 --> 00:54:06.891 First of all,

NOTE Confidence: 0.95907728

00:54:06.891 --> 00:54:08.133 not everybody is a candidate for

NOTE Confidence: 0.95907728

00:54:08.133 --> 00:54:09.546 the gamma knife and gamma knife

NOTE Confidence: 0.95907728

00:54:09.546 --> 00:54:10.706 does work really quite well,

NOTE Confidence: 0.95907728

00:54:10.710 --> 00:54:12.286 but there are risks.

NOTE Confidence: 0.95907728

00:54:12.286 --> 00:54:13.014 Radiation, necrosis,

NOTE Confidence: 0.95907728

00:54:13.014 --> 00:54:14.684 as Doctor Chang will attest

NOTE Confidence: 0.95907728

00:54:14.684 --> 00:54:16.650 to is is a problem,

NOTE Confidence: 0.95907728

00:54:16.650 --> 00:54:19.360 and there's a lot of a lot of it that occurs.

NOTE Confidence: 0.95907728

00:54:19.360 --> 00:54:20.896 And when disease comes back after the game,

NOTE Confidence: 0.95907728

00:54:20.900 --> 00:54:23.012 and if it's even harder to take care

NOTE Confidence: 0.95907728

00:54:23.012 --> 00:54:25.030 of and then there are the patients for

NOTE Confidence: 0.95907728

00:54:25.030 --> 00:54:27.084 which gamma knife is unfortunately not an

NOTE Confidence: 0.95907728

00:54:27.084 --> 00:54:28.956 option that require whole brain radiation.

NOTE Confidence: 0.95907728

00:54:28.960 --> 00:54:30.290 And even with our fancy

NOTE Confidence: 0.95907728

00:54:30.290 --> 00:54:31.354 spinning of the beams,
NOTE Confidence: 0.95907728

00:54:31.360 --> 00:54:33.420 hippocampal sparing in the manting,
NOTE Confidence: 0.95907728

00:54:33.420 --> 00:54:36.846 it carries risks of neurotoxicity so.
NOTE Confidence: 0.95907728

00:54:36.850 --> 00:54:38.544 I, I don't think there's any question.
NOTE Confidence: 0.95907728

00:54:38.550 --> 00:54:40.134 If there was a way to reduce the
NOTE Confidence: 0.95907728

00:54:40.134 --> 00:54:42.004 need for radiation or at least lower
NOTE Confidence: 0.95907728

00:54:42.004 --> 00:54:43.429 the dose of radiation required,
NOTE Confidence: 0.95907728

00:54:43.430 --> 00:54:45.496 that would make a big benefit for
NOTE Confidence: 0.95907728

00:54:45.496 --> 00:54:47.572 patients with breast cancer and brain
NOTE Confidence: 0.95907728

00:54:47.572 --> 00:54:49.509 metastases and other tumors as well.
NOTE Confidence: 0.95907728

00:54:49.510 --> 00:54:53.902 So we have already started looking.
NOTE Confidence: 0.95907728

00:54:53.902 --> 00:54:56.878 Into this and we have a DoD grant
NOTE Confidence: 0.95907728

00:54:56.878 --> 00:54:59.488 to help us conduct this work.
NOTE Confidence: 0.95907728

00:54:59.490 --> 00:55:01.730 I think DX one is perfectly poised to
NOTE Confidence: 0.95907728

00:55:01.730 --> 00:55:03.849 lower the needed dose of radiation,
NOTE Confidence: 0.95907728

00:55:03.850 --> 00:55:05.698 and I think radiation is perfectly

NOTE Confidence: 0.95907728

00:55:05.698 --> 00:55:08.210 poised to help the X one get into

NOTE Confidence: 0.95907728

00:55:08.210 --> 00:55:09.730 the brain nuts because remember.

NOTE Confidence: 0.95907728

00:55:09.730 --> 00:55:12.862 DX1 is looking for and using DNA to get

NOTE Confidence: 0.95907728

00:55:12.862 --> 00:55:15.332 into the tumors so dose of radiation

NOTE Confidence: 0.95907728

00:55:15.332 --> 00:55:17.210 to increase tumor death and release

NOTE Confidence: 0.95907728

00:55:17.273 --> 00:55:19.569 DNA should recruit more DX1 to the brain.

NOTE Confidence: 0.95907728

00:55:19.570 --> 00:55:21.082 Mets and the bar graphs are

NOTE Confidence: 0.95907728

00:55:21.082 --> 00:55:22.470 shown on the bottom there.

NOTE Confidence: 0.95907728

00:55:22.470 --> 00:55:24.724 That's so that's exactly what we see.

NOTE Confidence: 0.837978879

00:55:24.730 --> 00:55:25.434 We see the most.

NOTE Confidence: 0.837978879

00:55:25.434 --> 00:55:26.490 DX one get in the brain.

NOTE Confidence: 0.837978879

00:55:26.490 --> 00:55:28.758 Mets in the mice that get treated

NOTE Confidence: 0.837978879

00:55:28.758 --> 00:55:30.380 concurrently with the radiation.

NOTE Confidence: 0.837978879

00:55:30.380 --> 00:55:32.599 And take it to the obvious extreme.

NOTE Confidence: 0.837978879

00:55:32.600 --> 00:55:34.833 Those mice that get DX1 with the

NOTE Confidence: 0.837978879

00:55:34.833 --> 00:55:36.873 radiation also have the best response
NOTE Confidence: 0.837978879

00:55:36.873 --> 00:55:39.239 we see the less number of metastases,
NOTE Confidence: 0.837978879

00:55:39.240 --> 00:55:40.856 so it's all working the way we expect.
NOTE Confidence: 0.837978879

00:55:40.860 --> 00:55:43.120 I understand it's all preclinical,
NOTE Confidence: 0.837978879

00:55:43.120 --> 00:55:45.208 it's in mice, but sometimes things
NOTE Confidence: 0.837978879

00:55:45.208 --> 00:55:47.325 start to come together and it's
NOTE Confidence: 0.837978879

00:55:47.325 --> 00:55:49.293 it's looking very promising to me.
NOTE Confidence: 0.837978879

00:55:49.300 --> 00:55:50.804 Obviously very biased and.
NOTE Confidence: 0.837978879

00:55:50.804 --> 00:55:53.060 Very grateful to Benedet and Marta
NOTE Confidence: 0.837978879

00:55:53.123 --> 00:55:55.237 and Caroline and who for all their
NOTE Confidence: 0.837978879

00:55:55.237 --> 00:55:57.439 work with this it's it's been tough
NOTE Confidence: 0.837978879

00:55:57.440 --> 00:55:58.980 but we've hung through here and it's
NOTE Confidence: 0.837978879

00:55:58.980 --> 00:56:00.299 it's going really quite well now.
NOTE Confidence: 0.928401989166667

00:56:02.380 --> 00:56:04.165 And again, can't do any of this
NOTE Confidence: 0.928401989166667

00:56:04.165 --> 00:56:05.659 without help from your friends.
NOTE Confidence: 0.928401989166667

00:56:05.660 --> 00:56:08.090 I had to cross out the word little and say

NOTE Confidence: 0.928401989166667
00:56:08.155 --> 00:56:10.647 a lot because jangle from neurosurgery has.
NOTE Confidence: 0.928401989166667
00:56:10.650 --> 00:56:11.634 Been great friend and
NOTE Confidence: 0.928401989166667
00:56:11.634 --> 00:56:12.864 colleague to me for years.
NOTE Confidence: 0.928401989166667
00:56:12.870 --> 00:56:15.327 Now he is an expert in all things related
NOTE Confidence: 0.928401989166667
00:56:15.327 --> 00:56:17.722 to the brain and brain tumors and ways
NOTE Confidence: 0.928401989166667
00:56:17.722 --> 00:56:19.450 to treat tumors in the brain and he's
NOTE Confidence: 0.928401989166667
00:56:19.507 --> 00:56:21.109 helped us figure out these models.
NOTE Confidence: 0.928401989166667
00:56:21.110 --> 00:56:22.867 He's very interested in the dxy antibody.
NOTE Confidence: 0.928401989166667
00:56:22.870 --> 00:56:24.586 We work together all the time,
NOTE Confidence: 0.928401989166667
00:56:24.590 --> 00:56:26.144 but he also does some other things.
NOTE Confidence: 0.928401989166667
00:56:26.150 --> 00:56:27.406 Believe it or not,
NOTE Confidence: 0.928401989166667
00:56:27.406 --> 00:56:28.976 a lot of other things.
NOTE Confidence: 0.928401989166667
00:56:28.980 --> 00:56:31.056 And just recently had a great
NOTE Confidence: 0.928401989166667
00:56:31.056 --> 00:56:33.171 paper in nature cell biology where
NOTE Confidence: 0.928401989166667
00:56:33.171 --> 00:56:35.779 he reported on a new effect of an
NOTE Confidence: 0.928401989166667

00:56:35.780 --> 00:56:38.305 LRRC 31 protein that significantly
NOTE Confidence: 0.928401989166667

00:56:38.305 --> 00:56:40.325 sensitizes breast cancer brain
NOTE Confidence: 0.928401989166667

00:56:40.325 --> 00:56:42.298 metastases to radiation therapy.
NOTE Confidence: 0.928401989166667

00:56:42.300 --> 00:56:44.414 So it's almost like the universe is.
NOTE Confidence: 0.928401989166667

00:56:44.420 --> 00:56:47.580 Telling us something because that
NOTE Confidence: 0.928401989166667

00:56:47.580 --> 00:56:50.880 LRRC 31 protein is great.
NOTE Confidence: 0.928401989166667

00:56:50.880 --> 00:56:54.184 They can't cross the blood brain barrier.
NOTE Confidence: 0.928401989166667

00:56:54.190 --> 00:56:56.044 I think I just spent the last 20 minutes
NOTE Confidence: 0.928401989166667

00:56:56.044 --> 00:56:57.565 talking about an antibody that can
NOTE Confidence: 0.928401989166667

00:56:57.565 --> 00:56:59.770 carry things across the blood brain barrier.
NOTE Confidence: 0.928401989166667

00:56:59.770 --> 00:57:01.914 So we got the Hanson lab and the
NOTE Confidence: 0.928401989166667

00:57:01.914 --> 00:57:03.860 shower lab working together and we
NOTE Confidence: 0.928401989166667

00:57:03.860 --> 00:57:06.010 can put them together and make a
NOTE Confidence: 0.928401989166667

00:57:06.010 --> 00:57:09.098 DX1 LRRC 31 fusion protein that I'm
NOTE Confidence: 0.928401989166667

00:57:09.098 --> 00:57:11.290 hopeful is going to be next in line
NOTE Confidence: 0.928401989166667

00:57:11.354 --> 00:57:13.531 to cross over the river through the

NOTE Confidence: 0.928401989166667

00:57:13.531 --> 00:57:16.275 woods and into the brain and increase

NOTE Confidence: 0.928401989166667

00:57:16.275 --> 00:57:18.019 sensitivity to radiation therapy.

NOTE Confidence: 0.928401989166667

00:57:18.020 --> 00:57:21.180 So hopefully that was of some

NOTE Confidence: 0.928401989166667

00:57:21.180 --> 00:57:22.860 interest to people listening here.

NOTE Confidence: 0.928401989166667

00:57:22.860 --> 00:57:25.236 I have a lot of people to thank.

NOTE Confidence: 0.928401989166667

00:57:25.240 --> 00:57:27.262 Obviously jeongbang Zhao.

NOTE Confidence: 0.928401989166667

00:57:27.262 --> 00:57:28.610 Great colleague.

NOTE Confidence: 0.928401989166667

00:57:28.610 --> 00:57:28.933 Of.

NOTE Confidence: 0.928401989166667

00:57:28.933 --> 00:57:31.517 Joe Contessa and Marta Bero in his lab

NOTE Confidence: 0.928401989166667

00:57:31.517 --> 00:57:33.968 have been incredibly helpful to us.

NOTE Confidence: 0.928401989166667

00:57:33.970 --> 00:57:34.882 My own lab.

NOTE Confidence: 0.928401989166667

00:57:34.882 --> 00:57:36.706 I'm extremely grateful to your efforts.

NOTE Confidence: 0.928401989166667

00:57:36.710 --> 00:57:38.486 I'm I'm usually at the gamma knife nowadays,

NOTE Confidence: 0.928401989166667

00:57:38.490 --> 00:57:39.900 so you probably are wondering

NOTE Confidence: 0.928401989166667

00:57:39.900 --> 00:57:41.530 where I've been here I am.

NOTE Confidence: 0.928401989166667

00:57:41.530 --> 00:57:42.400 If you're looking for me,
NOTE Confidence: 0.928401989166667

00:57:42.400 --> 00:57:43.430 it still looks like me,
NOTE Confidence: 0.928401989166667

00:57:43.430 --> 00:57:43.797 right?
NOTE Confidence: 0.928401989166667

00:57:43.797 --> 00:57:45.999 And the Yale Gamma knife team
NOTE Confidence: 0.928401989166667

00:57:45.999 --> 00:57:47.949 everybody is is great help.
NOTE Confidence: 0.928401989166667

00:57:47.950 --> 00:57:49.595 I'm appreciative to everybody but
NOTE Confidence: 0.928401989166667

00:57:49.595 --> 00:57:51.548 last anyone that knows me knows
NOTE Confidence: 0.928401989166667

00:57:51.548 --> 00:57:53.556 that I'm a fan of the Marvel movies
NOTE Confidence: 0.928401989166667

00:57:53.556 --> 00:57:55.698 and the best part about the Marvel
NOTE Confidence: 0.928401989166667

00:57:55.698 --> 00:57:57.384 movies is always there's one more
NOTE Confidence: 0.928401989166667

00:57:57.384 --> 00:57:59.038 cut scene at the very end, right?
NOTE Confidence: 0.928401989166667

00:57:59.038 --> 00:58:00.478 And I think if you.
NOTE Confidence: 0.928401989166667

00:58:00.480 --> 00:58:02.020 Listen very carefully and you
NOTE Confidence: 0.928401989166667

00:58:02.020 --> 00:58:03.560 look off into the horizon.
NOTE Confidence: 0.928401989166667

00:58:03.560 --> 00:58:06.992 You will see that there is a team
NOTE Confidence: 0.928401989166667

00:58:06.992 --> 00:58:09.750 coming assembled led by Pi Megan King.

NOTE Confidence: 0.928401989166667
00:58:09.750 --> 00:58:11.170 Getting the best breast cancer,
NOTE Confidence: 0.928401989166667
00:58:11.170 --> 00:58:12.710 brains researchers together to
NOTE Confidence: 0.928401989166667
00:58:12.710 --> 00:58:14.635 expand and improve DNA targeted
NOTE Confidence: 0.928401989166667
00:58:14.635 --> 00:58:16.197 therapies towards better breast
NOTE Confidence: 0.928401989166667
00:58:16.197 --> 00:58:18.067 cancer treatment with Pat Larusso,
NOTE Confidence: 0.928401989166667
00:58:18.070 --> 00:58:19.870 Megan Kingaby Patel, Ryan Jensen,
NOTE Confidence: 0.928401989166667
00:58:19.870 --> 00:58:20.809 myself and Zhangzhou,
NOTE Confidence: 0.928401989166667
00:58:20.809 --> 00:58:22.687 and we're very thrilled to have
NOTE Confidence: 0.928401989166667
00:58:22.687 --> 00:58:23.550 been notified.
NOTE Confidence: 0.928401989166667
00:58:23.550 --> 00:58:25.485 Just recently that we've received
NOTE Confidence: 0.928401989166667
00:58:25.485 --> 00:58:27.420 the YCC Team Challenge Award
NOTE Confidence: 0.928401989166667
00:58:27.487 --> 00:58:28.799 to conduct this work.
NOTE Confidence: 0.928401989166667
00:58:28.800 --> 00:58:31.754 With that I will take a breath
NOTE Confidence: 0.928401989166667
00:58:31.754 --> 00:58:33.938 and stop talking and answer any
NOTE Confidence: 0.928401989166667
00:58:33.938 --> 00:58:34.730 questions if there are.
NOTE Confidence: 0.857410055555556

00:58:36.320 --> 00:58:39.803 Well, I think we're a little short on time,
NOTE Confidence: 0.857410055555556

00:58:39.810 --> 00:58:42.960 so it's it's exactly 1 now.
NOTE Confidence: 0.857410055555556

00:58:42.960 --> 00:58:45.660 James that was great.
NOTE Confidence: 0.857410055555556

00:58:45.660 --> 00:58:47.268 I'm certainly extraordinarily supportive
NOTE Confidence: 0.857410055555556

00:58:47.268 --> 00:58:50.559 of anyone who wants to study breast cancer.
NOTE Confidence: 0.857410055555556

00:58:50.560 --> 00:58:53.471 Brain tests is an area that I've
NOTE Confidence: 0.857410055555556

00:58:53.471 --> 00:58:55.158 thought about a lot over the years,
NOTE Confidence: 0.857410055555556

00:58:55.160 --> 00:58:59.261 and I would agree with you 100% that it's
NOTE Confidence: 0.857410055555556

00:58:59.261 --> 00:59:03.760 an area that's perhaps the most in need,
NOTE Confidence: 0.857410055555556

00:59:03.760 --> 00:59:04.888 and potentially the most
NOTE Confidence: 0.857410055555556

00:59:04.888 --> 00:59:06.298 in need in breast cancer.
NOTE Confidence: 0.857410055555556

00:59:06.300 --> 00:59:08.484 Because we we we may well be able
NOTE Confidence: 0.857410055555556

00:59:08.484 --> 00:59:10.260 to eradicate disease elsewhere in
NOTE Confidence: 0.857410055555556

00:59:10.260 --> 00:59:12.594 virtually everyone in the next decade.
NOTE Confidence: 0.857410055555556

00:59:12.600 --> 00:59:14.196 But the brain is the hardest place,
NOTE Confidence: 0.857410055555556

00:59:14.200 --> 00:59:15.679 it seems so.

NOTE Confidence: 0.857410055555556
00:59:15.679 --> 00:59:18.587 With that I wanna thank both
NOTE Confidence: 0.857410055555556
00:59:18.587 --> 00:59:21.209 both of you for great talks.
NOTE Confidence: 0.857410055555556
00:59:21.210 --> 00:59:23.146 It's been a great grand rounds and James.
NOTE Confidence: 0.857410055555556
00:59:23.150 --> 00:59:25.338 Congratulations on the on
NOTE Confidence: 0.857410055555556
00:59:25.338 --> 00:59:26.979 the challenge award.
NOTE Confidence: 0.970526285
00:59:27.970 --> 00:59:30.630 Thank you so much, alright?
NOTE Confidence: 0.713830828
00:59:30.630 --> 00:59:32.460 I made thanks again bye bye.
NOTE Confidence: 0.91101235
00:59:35.260 --> 00:59:38.000 And thanks to our audience.