

WEBVTT

NOTE duration:"00:06:04"

NOTE recognizability:0.789

NOTE language:en-us

NOTE Confidence: 0.885310881818182

00:00:05.420 --> 00:00:07.724 To put a historical perspective on

NOTE Confidence: 0.885310881818182

00:00:07.724 --> 00:00:09.850 the dramatic advances in biology,

NOTE Confidence: 0.885310881818182

00:00:09.850 --> 00:00:12.734 it's been during my lifetime that we

NOTE Confidence: 0.885310881818182

00:00:12.734 --> 00:00:15.341 learned the function of DNA as a first

NOTE Confidence: 0.885310881818182

00:00:15.341 --> 00:00:17.374 year student in college. In 1970,

NOTE Confidence: 0.885310881818182

00:00:17.374 --> 00:00:20.468 I saw a patient with multiple sclerosis,

NOTE Confidence: 0.885310881818182

00:00:20.470 --> 00:00:22.570 which at the time were thought to

NOTE Confidence: 0.885310881818182

00:00:22.570 --> 00:00:24.659 be mediated by the immune system.

NOTE Confidence: 0.885310881818182

00:00:24.660 --> 00:00:26.820 They were virtually no treatments

NOTE Confidence: 0.885310881818182

00:00:26.820 --> 00:00:29.488 I knew then. I wanted to dedicate

NOTE Confidence: 0.885310881818182

00:00:29.488 --> 00:00:30.856 my career to understanding.

NOTE Confidence: 0.885310881818182

00:00:30.860 --> 00:00:34.240 Disease and discover effective treatments.

NOTE Confidence: 0.885310881818182

00:00:34.240 --> 00:00:36.039 We've come a long way since the

NOTE Confidence: 0.885310881818182

00:00:36.039 --> 00:00:37.738 two major types of immune cells,
NOTE Confidence: 0.885310881818182

00:00:37.740 --> 00:00:38.940 T cells and B cells,
NOTE Confidence: 0.885310881818182

00:00:38.940 --> 00:00:40.780 were discovered around the time
NOTE Confidence: 0.885310881818182

00:00:40.780 --> 00:00:43.300 I saw my first Ms patient.
NOTE Confidence: 0.885310881818182

00:00:43.300 --> 00:00:45.328 There is a technique allowing us
NOTE Confidence: 0.885310881818182

00:00:45.328 --> 00:00:47.083 to visualize many different immune
NOTE Confidence: 0.885310881818182

00:00:47.083 --> 00:00:48.818 cell populations in the brain.
NOTE Confidence: 0.885310881818182

00:00:48.820 --> 00:00:50.050 So David, what are we looking
NOTE Confidence: 0.758046194285714

00:00:50.060 --> 00:00:52.475 at here? This is a Ms lesion,
NOTE Confidence: 0.758046194285714

00:00:52.480 --> 00:00:54.550 and all of these colored
NOTE Confidence: 0.758046194285714

00:00:54.550 --> 00:00:56.206 objects are individual cells
NOTE Confidence: 0.758046194285714

00:00:56.206 --> 00:00:58.479 that have different functions.
NOTE Confidence: 0.758046194285714

00:00:58.480 --> 00:01:00.810 And if you zoom in.
NOTE Confidence: 0.758046194285714

00:01:00.810 --> 00:01:03.066 Like so you see, for example,
NOTE Confidence: 0.758046194285714

00:01:03.070 --> 00:01:06.248 a immune cell at cell that directs
NOTE Confidence: 0.758046194285714

00:01:06.248 --> 00:01:09.038 a scavenger cell to devour mile.

NOTE Confidence: 0.728869063809524

00:01:09.390 --> 00:01:11.791 In Ms Research, an important event would

NOTE Confidence: 0.728869063809524

00:01:11.791 --> 00:01:14.071 allow us to deeply characterize those

NOTE Confidence: 0.728869063809524

00:01:14.071 --> 00:01:17.240 immune T cells and B cells without bias.

NOTE Confidence: 0.728869063809524

00:01:17.240 --> 00:01:20.280 We can now use a dramatic new technology

NOTE Confidence: 0.728869063809524

00:01:20.280 --> 00:01:23.466 called single cell RNA sequencing allows us

NOTE Confidence: 0.728869063809524

00:01:23.466 --> 00:01:26.250 to interrogate each individual immune cell.

NOTE Confidence: 0.728869063809524

00:01:26.250 --> 00:01:28.875 Examining the brain itself is too invasive,

NOTE Confidence: 0.728869063809524

00:01:28.880 --> 00:01:30.861 but we can access immune cells in

NOTE Confidence: 0.728869063809524

00:01:30.861 --> 00:01:33.200 the brain by examining spinal fluid,

NOTE Confidence: 0.728869063809524

00:01:33.200 --> 00:01:34.952 the liquid around the brain and

NOTE Confidence: 0.728869063809524

00:01:34.952 --> 00:01:36.687 spinal cord that tells us what

NOTE Confidence: 0.728869063809524

00:01:36.687 --> 00:01:38.223 immune cells are in the brain.

NOTE Confidence: 0.728869063809524

00:01:38.230 --> 00:01:40.834 We extract spinal fluid from a patient

NOTE Confidence: 0.728869063809524

00:01:40.834 --> 00:01:43.205 using a Spinal Tap by inserting

NOTE Confidence: 0.728869063809524

00:01:43.205 --> 00:01:45.170 a needle between the vertebrae

NOTE Confidence: 0.728869063809524

00:01:45.170 --> 00:01:47.510 and then collecting the fluid.
NOTE Confidence: 0.728869063809524

00:01:47.510 --> 00:01:48.182 Once extracted,
NOTE Confidence: 0.728869063809524

00:01:48.182 --> 00:01:50.870 the spinal fluid is rushed to the lab,
NOTE Confidence: 0.728869063809524

00:01:50.870 --> 00:01:53.150 where it's spun down to collect the cells,
NOTE Confidence: 0.728869063809524

00:01:53.150 --> 00:01:55.160 then brought to the 10X machine.
NOTE Confidence: 0.772631999259259

00:01:58.580 --> 00:02:01.247 We encapsulate each single T cell into
NOTE Confidence: 0.772631999259259

00:02:01.247 --> 00:02:03.943 a functionalized gel B as bar coded and
NOTE Confidence: 0.772631999259259

00:02:03.943 --> 00:02:06.308 mixed with enzymes and oils to create
NOTE Confidence: 0.772631999259259

00:02:06.308 --> 00:02:08.338 single cell microdroplets or gems.
NOTE Confidence: 0.772631999259259

00:02:08.340 --> 00:02:10.356 We then perform a chemical reaction
NOTE Confidence: 0.772631999259259

00:02:10.356 --> 00:02:12.397 to amplify the nucleic acid that
NOTE Confidence: 0.772631999259259

00:02:12.397 --> 00:02:14.305 codes for proteins that define each
NOTE Confidence: 0.772631999259259

00:02:14.305 --> 00:02:16.400 cell type to learn their function.
NOTE Confidence: 0.772631999259259

00:02:16.400 --> 00:02:18.878 The elegance of the technology is that
NOTE Confidence: 0.772631999259259

00:02:18.878 --> 00:02:20.834 we can identify cellular subtypes
NOTE Confidence: 0.772631999259259

00:02:20.834 --> 00:02:23.294 and rare cells with little bias,

NOTE Confidence: 0.772631999259259
00:02:23.300 --> 00:02:25.724 giving a big picture of the
NOTE Confidence: 0.772631999259259
00:02:25.724 --> 00:02:27.340 biology underlying the disease.
NOTE Confidence: 0.772631999259259
00:02:27.340 --> 00:02:30.946 This is what. We have discovered.
NOTE Confidence: 0.772631999259259
00:02:30.950 --> 00:02:32.833 Here we have a snapshot of the
NOTE Confidence: 0.772631999259259
00:02:32.833 --> 00:02:34.690 different and mean populations and the
NOTE Confidence: 0.772631999259259
00:02:34.690 --> 00:02:36.670 spinal fluid of a healthy subject,
NOTE Confidence: 0.772631999259259
00:02:36.670 --> 00:02:37.963 the blue dots,
NOTE Confidence: 0.772631999259259
00:02:37.963 --> 00:02:39.687 each representing immune cells
NOTE Confidence: 0.772631999259259
00:02:39.687 --> 00:02:41.909 with RNA signatures of the blood.
NOTE Confidence: 0.772631999259259
00:02:41.910 --> 00:02:44.334 The yellow dots are cells with
NOTE Confidence: 0.772631999259259
00:02:44.334 --> 00:02:46.470 RNA signatures of spinal fluid.
NOTE Confidence: 0.772631999259259
00:02:46.470 --> 00:02:48.798 As T cells traffic into the spinal fluid,
NOTE Confidence: 0.772631999259259
00:02:48.800 --> 00:02:51.260 they transition toward RNA signature.
NOTE Confidence: 0.772631999259259
00:02:51.260 --> 00:02:52.670 That's more nervous system like
NOTE Confidence: 0.772631999259259
00:02:52.670 --> 00:02:53.798 which is in green.
NOTE Confidence: 0.881410484285714

00:02:55.770 --> 00:02:57.378 Armed with what happens
NOTE Confidence: 0.881410484285714

00:02:57.378 --> 00:02:58.584 in healthy subjects,
NOTE Confidence: 0.881410484285714

00:02:58.590 --> 00:03:01.078 we can now look at patients with Ms.
NOTE Confidence: 0.881410484285714

00:03:01.080 --> 00:03:02.284 The lighter the color,
NOTE Confidence: 0.881410484285714

00:03:02.284 --> 00:03:03.488 the more the difference.
NOTE Confidence: 0.881410484285714

00:03:03.490 --> 00:03:05.214 Here we've identified the
NOTE Confidence: 0.881410484285714

00:03:05.214 --> 00:03:06.507 fundamental gene signatures
NOTE Confidence: 0.881410484285714

00:03:06.507 --> 00:03:08.519 that are different in patients
NOTE Confidence: 0.779773255555556

00:03:08.530 --> 00:03:10.855 with Ms an environmental event
NOTE Confidence: 0.779773255555556

00:03:10.855 --> 00:03:13.653 like an infection by common virus
NOTE Confidence: 0.779773255555556

00:03:13.653 --> 00:03:16.390 such as Epstein Barr virus or BV,
NOTE Confidence: 0.779773255555556

00:03:16.390 --> 00:03:19.192 may lead to the activation of
NOTE Confidence: 0.779773255555556

00:03:19.192 --> 00:03:21.670 autoreactive T cells recognizing myelin.
NOTE Confidence: 0.779773255555556

00:03:21.670 --> 00:03:23.325 These activated T cells that
NOTE Confidence: 0.779773255555556

00:03:23.325 --> 00:03:25.330 migrate into the brain where they.
NOTE Confidence: 0.779773255555556

00:03:25.330 --> 00:03:26.624 Cause inflammation.

NOTE Confidence: 0.779773255555556
00:03:26.624 --> 00:03:29.859 Blocking their migration with monoclonal
NOTE Confidence: 0.779773255555556
00:03:29.859 --> 00:03:31.800 antibodies markedly decreases.
NOTE Confidence: 0.779773255555556
00:03:31.800 --> 00:03:32.986 Ms attacks.
NOTE Confidence: 0.779773255555556
00:03:32.986 --> 00:03:35.358 Multiple sclerosis is a
NOTE Confidence: 0.779773255555556
00:03:35.358 --> 00:03:37.137 genetically mediated disease.
NOTE Confidence: 0.779773255555556
00:03:37.140 --> 00:03:40.836 We've identified 233 common genetic variants,
NOTE Confidence: 0.779773255555556
00:03:40.840 --> 00:03:42.976 each with a small effect on disease risk,
NOTE Confidence: 0.779773255555556
00:03:42.980 --> 00:03:45.176 but together lead to the disease.
NOTE Confidence: 0.779773255555556
00:03:45.180 --> 00:03:47.030 Majority of these common variants
NOTE Confidence: 0.779773255555556
00:03:47.030 --> 00:03:48.880 are controlling immune function and
NOTE Confidence: 0.779773255555556
00:03:48.943 --> 00:03:51.067 together contribute to a lower threshold
NOTE Confidence: 0.779773255555556
00:03:51.067 --> 00:03:52.920 for activating the immune system.
NOTE Confidence: 0.779773255555556
00:03:52.920 --> 00:03:55.349 It appears that B cells are critical.
NOTE Confidence: 0.779773255555556
00:03:55.350 --> 00:03:57.250 The activation of T cells.
NOTE Confidence: 0.779773255555556
00:03:57.250 --> 00:03:59.848 Perhaps related to the EBV virus,
NOTE Confidence: 0.779773255555556

00:03:59.850 --> 00:04:01.474 which infects B cells.
NOTE Confidence: 0.779773255555556

00:04:01.474 --> 00:04:04.451 Now the bleeding B cells also has
NOTE Confidence: 0.779773255555556

00:04:04.451 --> 00:04:06.751 a dramatic effect on stopping
NOTE Confidence: 0.779773255555556

00:04:06.751 --> 00:04:08.591 attacks in early disease.
NOTE Confidence: 0.779773255555556

00:04:08.600 --> 00:04:10.830 Here the monoclonal antibody is
NOTE Confidence: 0.779773255555556

00:04:10.830 --> 00:04:14.019 given to a patient every six months.
NOTE Confidence: 0.779773255555556

00:04:14.020 --> 00:04:16.260 We're now engaged in a clinical trial
NOTE Confidence: 0.779773255555556

00:04:16.260 --> 00:04:18.772 using B cell depletion at the very
NOTE Confidence: 0.779773255555556

00:04:18.772 --> 00:04:20.998 early stages of disease before there
NOTE Confidence: 0.779773255555556

00:04:21.069 --> 00:04:23.117 are any clinical manifestations.
NOTE Confidence: 0.779773255555556

00:04:23.120 --> 00:04:25.234 What advances that have been made since
NOTE Confidence: 0.779773255555556

00:04:25.234 --> 00:04:28.409 I saw my first patient with Ms Back in 1970.
NOTE Confidence: 0.779773255555556

00:04:28.409 --> 00:04:30.992 Back then we didn't know if the
NOTE Confidence: 0.779773255555556

00:04:30.992 --> 00:04:32.719 brain inflammation was secondary.
NOTE Confidence: 0.779773255555556

00:04:32.720 --> 00:04:35.464 Or causing Ms we now know the
NOTE Confidence: 0.779773255555556

00:04:35.464 --> 00:04:37.671 inflammation is causing the disease

NOTE Confidence: 0.779773255555556

00:04:37.671 --> 00:04:40.041 as immune modulation has dramatic

NOTE Confidence: 0.779773255555556

00:04:40.041 --> 00:04:42.430 effects on disease progression.

NOTE Confidence: 0.779773255555556

00:04:42.430 --> 00:04:44.260 We now know a significant number

NOTE Confidence: 0.779773255555556

00:04:44.260 --> 00:04:46.089 of the genes that cause Ms.

NOTE Confidence: 0.779773255555556

00:04:46.090 --> 00:04:48.080 They directly implicate the immune

NOTE Confidence: 0.779773255555556

00:04:48.080 --> 00:04:50.070 system and initiating the disease.

NOTE Confidence: 0.779773255555556

00:04:50.070 --> 00:04:50.822 Most importantly,

NOTE Confidence: 0.779773255555556

00:04:50.822 --> 00:04:53.454 in 1970 we had no treatments for

NOTE Confidence: 0.779773255555556

00:04:53.454 --> 00:04:56.138 Ms Now we have highly effective

NOTE Confidence: 0.779773255555556

00:04:56.138 --> 00:04:58.730 treatments that stop disease flare ups.

NOTE Confidence: 0.779773255555556

00:04:58.730 --> 00:05:01.018 Do we know the cause of Ms while

NOTE Confidence: 0.779773255555556

00:05:01.018 --> 00:05:03.319 science does not truly prove causality.

NOTE Confidence: 0.779773255555556

00:05:03.320 --> 00:05:05.522 We make models that are constantly

NOTE Confidence: 0.779773255555556

00:05:05.522 --> 00:05:08.110 refined and tested by clinical trials.

NOTE Confidence: 0.779773255555556

00:05:08.110 --> 00:05:10.500 These models provide the most

NOTE Confidence: 0.779773255555556

00:05:10.500 --> 00:05:12.412 convincing evidence for causality.
NOTE Confidence: 0.779773255555556

00:05:12.420 --> 00:05:14.618 While we have a good working model
NOTE Confidence: 0.779773255555556

00:05:14.618 --> 00:05:16.260 for early relapsing mitting Ms,
NOTE Confidence: 0.779773255555556

00:05:16.260 --> 00:05:18.450 we have little insight into the
NOTE Confidence: 0.779773255555556

00:05:18.450 --> 00:05:20.500 progressive phase of the disease.
NOTE Confidence: 0.779773255555556

00:05:20.500 --> 00:05:22.792 We also don't know yet whether
NOTE Confidence: 0.779773255555556

00:05:22.792 --> 00:05:24.836 early treatment would be cell
NOTE Confidence: 0.779773255555556

00:05:24.836 --> 00:05:26.612 depletion prevents evolution to
NOTE Confidence: 0.779773255555556

00:05:26.612 --> 00:05:28.832 the progressive form of Ms.
NOTE Confidence: 0.779773255555556

00:05:28.840 --> 00:05:31.318 However, our examination of spinal fluid,
NOTE Confidence: 0.779773255555556

00:05:31.320 --> 00:05:33.375 these powerful new single cell
NOTE Confidence: 0.779773255555556

00:05:33.375 --> 00:05:34.608 technologies has revealed
NOTE Confidence: 0.779773255555556

00:05:34.608 --> 00:05:36.195 previously unknown pathways found
NOTE Confidence: 0.779773255555556

00:05:36.195 --> 00:05:37.950 in the infiltrating immune cells
NOTE Confidence: 0.779773255555556

00:05:37.950 --> 00:05:39.719 that are causing the disease.
NOTE Confidence: 0.779773255555556

00:05:39.720 --> 00:05:42.680 It will take years to put these new

NOTE Confidence: 0.779773255555556

00:05:42.680 --> 00:05:45.416 experiments into a more refined model of Ms,

NOTE Confidence: 0.779773255555556

00:05:45.420 --> 00:05:47.688 but this is an incredibly exciting time

NOTE Confidence: 0.779773255555556

00:05:47.688 --> 00:05:50.535 in the study of this disease and of neuro.

NOTE Confidence: 0.779773255555556

00:05:50.540 --> 00:05:51.410 Degeneration.