WEBVTT

NOTE duration: ”00:03:52.618”

NOTE Confidence: 0.9005127

00:00:07.279 --> 00:00:08.580 In the small intestine,

NOTE Confidence: 0.9722317

00:00:09.119 --> 00:00:10.320 which is the majority of

NOTE Confidence: 0.9722317

00:00:10.320 --> 00:00:12.480 your digestive tract, you have

NOTE Confidence: 0.9722317

00:00:12.480 --> 00:00:14.325 crypts and villi. So villi

NOTE Confidence: 0.9722317

00:00:14.325 --> 00:00:15.605 are these finger like projections

NOTE Confidence: 0.9722317

00:00:15.605 --> 00:00:16.585 that stick out.

NOTE Confidence: 0.99189454

00:00:17.285 --> 00:00:19.064 They're important for nutrient absorption.

NOTE Confidence: 0.9824829

00:00:19.845 --> 00:00:21.685 A crypt is the intestinal

NOTE Confidence: 0.9824829

00:00:21.685 --> 00:00:22.664 stem cell niche.

NOTE Confidence: 0.9897461

00:00:22.965 --> 00:00:24.585 It's just this cute little

NOTE Confidence: 0.9897461

00:00:24.645 --> 00:00:25.145 cup

NOTE Confidence: 0.93777186

00:00:25.525 --> 00:00:26.805 that sits in the intestine

NOTE Confidence: 0.93777186

00:00:26.805 --> 00:00:27.605 and the stem cells sit

NOTE Confidence: 0.93777186

00:00:27.605 --> 00:00:28.485 at the very bottom of

NOTE Confidence: 0.93777186

00:00:28.485 --> 00:00:29.580 it, and that forms during

NOTE Confidence: 0.93777186

00:00:29.660 --> 00:00:30.400 during development.

NOTE Confidence: 0.96453583

00:00:31.980 --> 00:00:33.180 What happens in a crypt?

NOTE Confidence: 0.96453583

00:00:33.180 --> 00:00:34.220 So many things happen in

NOTE Confidence: 0.96453583

00:00:34.220 --> 00:00:35.420 a crypt. The intestinal stem

NOTE Confidence: 0.96453583

00:00:35.420 --> 00:00:36.540 cells sit at the bottom,

NOTE Confidence: 0.96453583

00:00:36.540 --> 00:00:37.500 and they divide, and they

NOTE Confidence: 0.96453583

00:00:37.500 --> 00:00:39.420 make daughter cells, progeny, that

NOTE Confidence: 0.96453583

00:00:39.420 --> 00:00:40.380 can then move up the

NOTE Confidence: 0.96453583

00:00:40.380 --> 00:00:41.420 crypt. And once they move

NOTE Confidence: 0.96453583

00:00:41.420 --> 00:00:42.755 up the crypt, they're going

NOTE Confidence: 0.96453583

00:00:42.755 --> 00:00:43.955 to lose their ability to

NOTE Confidence: 0.96453583

00:00:43.955 --> 00:00:45.555 divide anymore, and they're gonna

NOTE Confidence: 0.96453583

00:00:45.555 --> 00:00:46.595 move into the villus, which

NOTE Confidence: 0.96453583

00:00:46.595 --> 00:00:48.455 are these these nutrient absorbers.

NOTE Confidence: 0.9842413

00:00:48.835 --> 00:00:50.034 And so every cell starts

NOTE Confidence: 0.9842413

00:00:50.034 --> 00:00:50.915 in a crypt, and it

NOTE Confidence: 0.9842413

00:00:50.915 --> 00:00:51.635 gets to the tip of

NOTE Confidence: 0.9842413

00:00:51.635 --> 00:00:52.515 the villus within a few

NOTE Confidence: 0.9842413

00:00:52.515 --> 00:00:53.315 days, and then it dies,

NOTE Confidence: 0.9842413

00:00:53.315 --> 00:00:54.275 and its job is done.

NOTE Confidence: 0.9842413

00:00:54.275 --> 00:00:55.075 And so it's a really

NOTE Confidence: 0.9842413

00:00:55.075 --> 00:00:57.155 fast process that's happening all

NOTE Confidence: 0.9842413

00:00:57.155 --> 00:00:57.660 the time.

NOTE Confidence: 0.9557495

00:01:02.540 --> 00:01:03.980 Our goal is to understand

NOTE Confidence: 0.9557495

00:01:03.980 --> 00:01:05.280 how cellular behaviors

NOTE Confidence: 0.99560547

00:01:05.660 --> 00:01:06.720 and function

NOTE Confidence: 0.99853516

00:01:07.100 --> 00:01:08.800 converge with physical forces

NOTE Confidence: 0.9633977

00:01:09.260 --> 00:01:10.860 to generate functional tissue, both

NOTE Confidence: 0.9633977

00:01:10.860 --> 00:01:12.060 in development. And then once

NOTE Confidence: 0.9633977

00:01:12.060 --> 00:01:13.635 you generate this structure, how

NOTE Confidence: 0.9633977

00:01:13.635 --> 00:01:15.235 do you maintain it? Shape

NOTE Confidence: 0.9633977

00:01:15.235 --> 00:01:16.834 is part of function. It's

NOTE Confidence: 0.9633977

00:01:16.834 --> 00:01:17.715 not just some sort of

NOTE Confidence: 0.9633977

00:01:17.715 --> 00:01:19.075 passive thing that happens. It's

NOTE Confidence: 0.9633977

00:01:19.075 --> 00:01:21.175 actually really contributing to

NOTE Confidence: 0.97043747

00:01:21.635 --> 00:01:23.715 how cells sense and respond

NOTE Confidence: 0.97043747

00:01:23.715 --> 00:01:25.315 to their environment. So we

NOTE Confidence: 0.97043747

00:01:25.315 --> 00:01:26.595 know that the the stem

NOTE Confidence: 0.97043747

00:01:26.595 --> 00:01:28.275 cells in the crypt require

NOTE Confidence: 0.97043747

00:01:28.275 --> 00:01:29.709 certain signals to see certain

NOTE Confidence: 0.97043747

00:01:29.709 --> 00:01:30.829 signals and respond to certain

NOTE Confidence: 0.97043747

00:01:30.829 --> 00:01:32.689 signals to both maintain

NOTE Confidence: 0.9791215

00:01:33.310 --> 00:01:34.350 their identity as a stem

NOTE Confidence: 0.9791215

00:01:34.350 --> 00:01:35.390 cell, but also to know

NOTE Confidence: 0.9791215

00:01:35.390 --> 00:01:37.229 when to divide. And if

NOTE Confidence: 0.9791215

00:01:37.229 --> 00:01:38.350 you start messing with the

NOTE Confidence: 0.9791215

00:01:38.350 --> 00:01:39.789 shape of that crypt, they

NOTE Confidence: 0.9791215

00:01:39.789 --> 00:01:41.390 see signals differently because now

NOTE Confidence: 0.9791215

00:01:41.390 --> 00:01:42.850 they're exposed to them differently.

NOTE Confidence: 0.9791215

00:01:43.005 --> 00:01:44.625 There's all this constant turnover.

NOTE Confidence: 0.9791215

00:01:44.924 --> 00:01:45.805 How do we actually make

NOTE Confidence: 0.9791215

00:01:45.805 --> 00:01:46.924 sure that cells are doing

NOTE Confidence: 0.9791215

00:01:46.924 --> 00:01:47.884 what they're supposed to do

NOTE Confidence: 0.9791215

00:01:47.884 --> 00:01:49.005 all the time? And we've

NOTE Confidence: 0.9791215

00:01:49.005 --> 00:01:50.365 been really discovering these new

NOTE Confidence: 0.9791215

00:01:50.365 --> 00:01:51.485 patterns in the intestine that

NOTE Confidence: 0.9791215

00:01:51.485 --> 00:01:52.945 we didn't know existed before.

NOTE Confidence: 0.9791215

00:01:53.005 --> 00:01:54.604 We wanna understand how do

NOTE Confidence: 0.9791215

00:01:54.604 --> 00:01:56.304 they contribute to the intestines

NOTE Confidence: 0.9791215

00:01:56.524 --> 00:01:58.384 function as this nutrient absorber.

NOTE Confidence: 0.98316956

00:02:03.620 --> 00:02:05.160 We're really big into microscopy.

NOTE Confidence: 0.98316956

00:02:05.380 --> 00:02:07.160 We do live tissue imaging

NOTE Confidence: 0.98316956

00:02:07.380 --> 00:02:09.300 and also three d quantitative

NOTE Confidence: 0.98316956

00:02:09.300 --> 00:02:09.800 microscopy

NOTE Confidence: 0.9583083

00:02:10.260 --> 00:02:11.300 as well as we use

NOTE Confidence: 0.9583083

00:02:11.300 --> 00:02:13.380 intestinal organoid models to do

NOTE Confidence: 0.9583083

00:02:13.380 --> 00:02:14.760 more mechanistic studies.

NOTE Confidence: 0.9595811

00:02:15.585 --> 00:02:16.865 We've been getting really into

NOTE Confidence: 0.9595811

00:02:16.865 --> 00:02:19.685 biophysics lately and understanding how

NOTE Confidence: 0.9595811

00:02:19.745 --> 00:02:21.685 cells are sort of sensing

NOTE Confidence: 0.9595811

00:02:21.745 --> 00:02:23.185 or responding to these forces

NOTE Confidence: 0.9595811

00:02:23.185 --> 00:02:23.985 like I said, and we

NOTE Confidence: 0.9595811

00:02:23.985 --> 00:02:25.425 think that tissue architecture is

NOTE Confidence: 0.9595811

00:02:25.425 --> 00:02:26.385 really important in that. So

NOTE Confidence: 0.9595811

00:02:26.385 --> 00:02:27.425 the shape of the intestine

NOTE Confidence: 0.9595811

00:02:27.425 --> 00:02:28.110 actually contributes

NOTE Confidence: 0.9124046

00:02:29.230 --> 00:02:30.830 a lot to the turnover

NOTE Confidence: 0.9124046

00:02:30.830 --> 00:02:31.558 of the cells or how

NOTE Confidence: 0.9124046

00:02:31.558 --> 00:02:31.870 they're behaving and moving. We're

NOTE Confidence: 0.9124046

00:02:31.870 --> 00:02:33.550 really excited about understanding how

NOTE Confidence: 0.9124046

00:02:33.550 --> 00:02:34.990 the biophysical principles of the

NOTE Confidence: 0.9124046

00:02:34.990 --> 00:02:36.450 tissue and the cellular behaviors

NOTE Confidence: 0.9124046

00:02:36.510 --> 00:02:38.130 can actually help us understand

NOTE Confidence: 0.9124046

00:02:38.190 --> 00:02:40.030 how to heal faster in

NOTE Confidence: 0.9124046

00:02:40.030 --> 00:02:41.490 these degenerative conditions.

NOTE Confidence: 0.9733244

00:02:46.935 --> 00:02:48.555 These can be really relevant

NOTE Confidence: 0.9733244

00:02:48.615 --> 00:02:50.615 in disease like cancer where

NOTE Confidence: 0.9733244

00:02:50.615 --> 00:02:52.135 you have not enough turnover

NOTE Confidence: 0.9733244

00:02:52.135 --> 00:02:53.275 and too much proliferation

NOTE Confidence: 0.9161018

00:02:53.975 --> 00:02:56.190 or in inflammatory conditions like

NOTE Confidence: 0.9161018

00:02:56.190 --> 00:02:58.030 IBD or even autoimmune like

NOTE Confidence: 0.9161018

00:02:58.030 --> 00:02:59.950 celiac where you're losing too

NOTE Confidence: 0.9161018

00:02:59.950 --> 00:03:00.770 many cells.

NOTE Confidence: 0.993571

00:03:01.230 --> 00:03:02.590 The hope is, of course,

NOTE Confidence: 0.993571

00:03:02.590 --> 00:03:03.790 can we sort of use

NOTE Confidence: 0.993571

00:03:03.790 --> 00:03:04.530 these principles

NOTE Confidence: 0.92464197

00:03:04.910 --> 00:03:05.730 as therapeutics?

NOTE Confidence: 0.9413385

00:03:06.350 --> 00:03:07.630 Not to necessarily treat the

NOTE Confidence: 0.9413385

00:03:07.630 --> 00:03:09.630 underlying disease, but for example,

NOTE Confidence: 0.9413385

00:03:09.630 --> 00:03:10.370 in IBD,

NOTE Confidence: 0.98435694

00:03:10.670 --> 00:03:11.685 you have all of this

NOTE Confidence: 0.98435694

00:03:11.925 --> 00:03:13.525 inflammatory response happening, and then

NOTE Confidence: 0.98435694

00:03:13.525 --> 00:03:14.885 that decreases barrier function of

NOTE Confidence: 0.98435694

00:03:14.885 --> 00:03:15.925 your gut because you're losing

NOTE Confidence: 0.98435694

00:03:15.925 --> 00:03:16.885 all these cells, which then

NOTE Confidence: 0.98435694

00:03:16.885 --> 00:03:17.944 increases inflammation.

NOTE Confidence: 0.99624634

00:03:18.565 --> 00:03:19.364 If we can make the

NOTE Confidence: 0.99624634

00:03:19.364 --> 00:03:21.605 epithelial cells stop responding and

NOTE Confidence: 0.99624634

00:03:21.605 --> 00:03:23.364 actually heal and make a

NOTE Confidence: 0.99624634

00:03:23.364 --> 00:03:24.805 new barrier, can we actually

NOTE Confidence: 0.99624634

00:03:24.805 --> 00:03:26.665 dampen that inflammatory response?

NOTE Confidence: 0.9907064

00:03:27.740 --> 00:03:28.860 I think Yale is one

NOTE Confidence: 0.9907064

00:03:28.860 --> 00:03:30.320 of the most collaborative environments

NOTE Confidence: 0.9907064

00:03:30.380 --> 00:03:31.840 and places I've ever been.

NOTE Confidence: 0.9811346

00:03:32.220 --> 00:03:34.139 Yale has a really deep,

NOTE Confidence: 0.9811346

00:03:34.139 --> 00:03:35.760 strong history in cell biology,

NOTE Confidence: 0.9811346

00:03:35.820 --> 00:03:36.320 cytoskeleton,

NOTE Confidence: 0.95198566

00:03:36.940 --> 00:03:38.160 and also genetics

NOTE Confidence: 0.8783366

00:03:38.540 --> 00:03:40.000 and quantitative biology,

NOTE Confidence: 0.9914822

00:03:40.475 --> 00:03:41.834 allowing me to interface with

NOTE Confidence: 0.9914822

00:03:41.834 --> 00:03:43.194 different fields and can actually

NOTE Confidence: 0.9914822

00:03:43.194 --> 00:03:44.555 push our research further and

NOTE Confidence: 0.9914822

00:03:44.555 --> 00:03:45.615 in different directions.