Science Magazine Podcast
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Music

Host – Kerry Klein
Welcome to the *Science* Podcast for October 12th, 2012. I'm Kerry Klein.

Host – Sarah Crespi
And I'm Sarah Crespi. This week: mutation rates and the pace of human history [14:21], hidden patterns in scientific publishing [23:48], and a look at the deep history of animal development [00:57]…

Interviewee – Stuart Newman
You have to turn back the clock and look at what forces were acting on the very primitive aggregates of cells that were present about half a billion years ago when animals first arose.

Host – Kerry Klein
Plus, a few stories from our online daily news site [35:01].

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Music ends

[00:57]
Host – Sarah Crespi
More than half a billion years ago, a new material appeared on Earth—clumps of cells that adhered to each other, sometimes acting like a liquid and other times like a solid. The physical properties of this new substance set the stage for the physical forms of multicellular organisms. I spoke with Stuart Newman about how the properties and forces inherent in this material still hold sway in patterns of animal development.

Interviewee – Stuart Newman
In all of the different types of animals, there is development from a cluster of cells of layers of tissue, and these layers are generally non-intermixing. We also generate interior spaces – cavities. And when the embryo organizes itself, it elongates often, not always; it generates appendages from the surface; and there are segments that form in many different types of animals that are not directly related to each other. And what I mean by that is that sometimes you see segmented forms in disparate phyla that don't have a common ancestor that was segmented. So I call these different forms and structures

morphological motifs. And not every one of them is present in every type of animal, but there's a limited number of them, and every type of animal is organized with at least several of these motifs.

Interviewer – Sarah Crespi
So, as you say, they're common to a lot of different animals. How far back in time do these motifs hold? I mean, when did they arise?

Interviewee – Stuart Newman
So there were two what are called explosive diversification periods. One began maybe 640 million years ago, and one around 540 million years ago. The first one was called the Ediacaran explosion, and the second one the Cambrian explosion. And it's thought that these diversification events, each of them were confined to maybe 10-20 million years. So this happened rapidly, geologically speaking, but more than half a billion years ago.

Interviewer – Sarah Crespi
And so what are some ideas about how these shared motifs might have arisen from our single-celled ancestors?

Interviewee – Stuart Newman
There was several billion years of evolution that led to the single-celled ancestors of the animals. So these cells were quite sophisticated and adapted to their own single-cell life. Then something happened that allowed cells to cluster. And what we know is that the genes that mediate clustering of cells in all of the modern animals – they're called cadherins, or at least cadherins are the major group of such proteins. They existed in these single-celled organisms, and they were used for single-cell functions – for perhaps capturing prey or adhering to the substratum. But they weren't used to coordinate multicellular development because there were no multicellular organisms. But then these cadherins and similar types of proteins were recruited for homophilic interaction, and homotypic interaction of clustering of cells. And then you had basically a form of matter that previously didn't exist in the biological world. Because you have these subunits that are independently mobile – they're not fixed in their position – but they are also cohesive. So, in a sense, this new type of material is like a liquid, because a liquid is defined by subunits – molecules in the case of nonliving liquids – that are mobile but nonetheless cohesive. So when you have this new type of living matter, then it can do things that liquids do. So, for example, if you have populations of cells that have different amounts or different types of these surface proteins, they can separate out like oil and water, and then you can have multiple layers. That's a morphological step that can just take place because of some mutational change in the expression of these molecules. So you get new forms. And these new forms don't necessarily arise because they're better adapted to anything, they just arise because of the inherent material properties of these clusters of cells. Every cell – bacteria, and in unicellular eukaryotic cells – they have oscillators within them. That is, they have biochemical networks that change periodically with time. It seems to be just a spontaneous property of complex networks that you often get oscillations. But we know from the study of coupling of oscillators in nonliving systems

that oscillators don't have to be specifically interacting with each other; they can be just nonspecifically interacting, and they come into synchrony. But when it happens in a cluster of cells, then the cells achieve a uniform state across fairly large distances, or distances of many cells. So it's a way of bringing cells into biochemical coordination. Now if the cells receive some kind of external signal or some signal within the mass, they're all at the same state and they can all react in concert. And this is very interesting because it's a purely physical effect, but it creates what embryologists in the past called developmental fields, or embryonic fields. A field is a system of cells that are coordinated with one another across distances within the embryo. So that's another thing that could happen. But if you have oscillations and coordination like this, the oscillations could also locally come out of phase with each other, and you can get segmentation to occur. Again, these are manifestations of material properties of clusters of cells that give rise to forms based on physical processes that are applied to the nonliving and living world, but these forms then can exist in the biosphere and find appropriate niches. Maybe segmentation is useful for something, so segmented forms will find the niche where they can exist. But the segments did not come about because of adaptation; the segments came about because of the inherent physical properties of the tissue.

Interviewer – Sarah Crespi
Well let's come at this from a different angle. We've talked a little bit about why these things are held in common, but where is the novelty? Why haven't we seen new patterns of development arise?

Interviewee – Stuart Newman
Every material has its inherent properties, and although those properties may not always be manifested, when they are manifested there's a limit to how many different types of things you can get out of it. And then similarly with clusters of animal cells, they can manifest a number of different motifs, but it's not unlimited as to what they can form. So in a way, this potential was exhausted early on. If physical forces characteristic of this kind of – it's called the mesoscale materials. It's middle-scale. It's not microscopic or molecular, and it's not cosmological, but it's middle-scale. These middle-scale processes can give rise to layers, to interior spaces, to segments. They can elongate if the subunits have certain properties. It turns out that among the genes that were present in the single-celled ancestors, there were a number of genes that were capable of mobilizing these physical forces of the middle scale when the cells found themselves in clusters. Before that, that kind of physics was irrelevant to the individual cell, but in the cluster, it became relevant. So then because these molecules were already there, they didn't have to newly evolve – you know, this explosive diversification of body plans and forms – when this first happened, and then you really can't get much more after that. But what you can do is you can stick with those forms, and you can reinforce them by further genetic evolution; you can integrate them with one another. There are many things that have happened in the last half a billion years. But among the things that have happened is not the production of new forms, because the era of morphological diversification basically has passed, and now we're just building on those templates.

Interviewer – Sarah Crespi

Really interesting. So your article's actually part of a special issue on how forces work in development. Can you talk a bit about how tension and adhesion play a role in development?

Interviewee – Stuart Newman
In the individual single cells, you might have adhesion molecules on their surfaces. And you also have tension in individual cells because every cell has a cytoskeleton that tugs from the inside on its surface. Now if you have a cluster of cells, the basis of the clustering is adhesion. You can get separation in two different layers because of differential adhesion, but you can also get cells kind of tugging from the inside and pulling away from each other, and that basically complicates things. In a nonliving liquid, nothing is tugging from inside the molecule to pull the individual molecules away from each other. So this is basically a unique characteristic of the kinds of liquid-like materials that a cluster of cells represent, because it has this internal tugging that can change the balance of forces and make something that would normally mix because of similar adhesive properties. Maybe because the cells are tugging from the inside, they don't mix as well. And then cells also do something else that we don't see in the nonliving world. They can produce signals that repel other cells. So in a way, there are things about embryos that you would never really infer from looking at nonliving materials, but once you see the forces that are generated by cells interacting with each other, you can almost easily understand, based on physics, what the cells are doing in the embryo.

Interviewer – Sarah Crespi
Great. Alright, well Stuart Newman, thanks so much for talking with me.

Interviewee – Stuart Newman
Thank you.

Host – Sarah Crespi
Stuart Newman and colleagues write on the evolution of developmental motifs in a special issue this week on the role of mechanical forces in development. You can read more articles on this theme at www.sciencemag.org/special/forces.

Music

[12:24]
Host – Kerry Klein
In 1950, the psychiatrist and so-called "catastrophist" Immanuel Velikovsky published a book entitled *Worlds in Collision*, in which he postulated that close encounters between the Earth and other planets were responsible for many catastrophic events mentioned in mythologies and religious texts. A few decades later, AAAS hosted a symposium to debate the veracity of Velikovsky's claims and to discuss the relationship between independent scholars and the scientific community. Among the list of speakers, renowned astronomer Carl Sagan weighed in on the discussion. Here's a clip of his talk.

Recording – Carl Sagan
The recent criticism of a prevailing belief is a service to the proponents of that belief, because if they are incapable of defending it, they are well advised to abandon it. This self-questioning and error-correcting aspect of science is its most striking property, and sets it off from many other areas of human endeavor, such as politics and theology. The idea of science as a method rather than a body of knowledge is not widely appreciated outside of science or indeed in, I'm sorry to say, in some of the corridors inside of science. For this reason, I and some other of my colleagues in the AAAS have advocated a regular set of discussions at the annual AAAS meeting of hypotheses which are on the borderlines of science or which have attracted substantial public interest. The idea is not to attempt to definitely to settle such an issue, but to illustrate the process of reasoned disputation, and hopefully to show how scientists approach a problem which does not lend itself to crisp experimentation or is unorthodox in its interdisciplinary nature or otherwise evokes strong emotions.

Host – Kerry Klein
Audio recordings of Carl Sagan, Immanuel Velikovsky, and others accompany a review this week of a book called *The Pseudoscience Wars*. You can hear the rest of the recordings online with the book review at www.sciencemag.org.

Music

[14:21]
Host – Sarah Crespi
The mutants of X-Men and other fantasy future humans may have to wait, as new research suggests that rates of human mutation may be slower than we once thought. Contributing correspondent Ann Gibbons spoke with Edward Hurme about how changing the estimated rate may force a rewrite of our evolutionary history.

Interviewee – Ann Gibbons
So the mutation rate is a simple thing. It's the number of mutations that arise between two parents and their child. So I have children. It's how many mutations each of my children has that are new between what I had and what my husband had. The new breakthrough is that this rate can now be determined much more precisely than it ever had been determined before by sequencing the genome of many living humans. And when you actually sequence the genomes of trios of parents – so two parents and their child – researchers in nine different studies have come up with a very precise measurement of what that mutation rate is. And the number they come up with – about 36 new mutations in each newborn across the entire genome.

Interviewer – Edward Hurme
So why was this so hard to measure before? What are some of the challenges involved in measuring the mutation rates?

Interviewee – Ann Gibbons

Well, in the past, we couldn't get good enough coverage of the human genome to count the number of mutations because the estimates of the human genome sequence were rough drafts. So you couldn't be sure that you were counting all the mutations that arose between a parent and child. So what scientists did – because they couldn't measure the mutation rate directly in living people – they would take a gene lineage. They would take a region of the genome – just whatever region they had studied, like an important gene that was in chimpanzees and humans – and they would count the number of mutations that differed between chimps and humans, or humans and macaques, or some other primate, and then they would build a family tree of sorts. And that would give them sort of the relative distance genetically between different species. They would then time the root of that tree by using fossils. So they'd figure, say you had a certain number of mutations between a human and a chimp, you might look at the fossils of the earliest members of the human family and see that they all lived between about four and seven million years ago. That would give you a rough rate if you divided the number of mutations by the number of years. There were a number of problems with this method, and one of them was that we didn't have any fossils of chimpanzees or gorillas, and it was unclear if you had exactly the right dates for the fossils; were they dated precisely; and were the oldest fossils of humans or the oldest fossils of other primates actually alive pretty closely to when they arose? One of the problems is that when you find a fossil of an early human ancestor, for example, one, is it really a human ancestor or is it an ancestor of a chimp and we don't know that or some other extinct species? So the fossils we have that we think are the earliest members of the human family may not be. Or, even if they are actually members of the human family, maybe they lived one or two or three million years after the first members arose, and the fossil record doesn't reflect everything that's out there.

Interviewer – Edward Hurme
So the new findings suggest that human mutation rates are actually slower than we previously thought. Why is this important?

Interviewee – Ann Gibbons
We use the mutation rate for everything from when did our ancestors split from the lineage that led to chimpanzees – you know, we come up with estimates that range between five and seven million years, some a little earlier. We use them to date everything like when we split from the ancestors of Neanderthals or when we split from the ancestors of this new kind of human – the Denisovans – that were from Russia. We use it to date when modern humans came out of Africa. And the idea has been that it's been in the last 60,000 years that our ancestors swept out of Africa and replaced Neandertals and other species. And even way back in primate evolution, it's used to date, for example, when the first apes appeared in Africa. When did early apes split from monkeys – the ancestors of monkeys? When did the first African apes appear in Africa? So as you can see, our whole sense of timing in human evolution and primate evolution comes from these rates. And the reason timing's important is many hypotheses hinge on why do we suddenly see new species of upright-walking hominids? Why do they appear? Well, maybe there's a difference in the climate. So if you want to see if there

are changes in the climates, you need a date for when the first members of the human family arose.

Interviewer – Edward Hurme
How have researchers and anthropologists reacted to these new dates?

Interviewee – Ann Gibbons
Eight new studies in the past three years, and an older study, have all calculated the mutation rate directly. This is sort of the result of new high-throughput genome sequencing methods that give you high-quality coverage of the entire genome. So we're able to get the more precise rate, which we sort of said is about an average of 36 mutations in each newborn. That's something like a chance of getting 1.2 mutations per nucleotide site per 100 million years, okay? So when you think about spreading 36 mutations over three billion nucleic acids or bases in your genome, it comes out to not very many mutations per generation. This is the average rate in modern humans per generation, and it can be converted into a rate per year. Now there's a little debate about how you do that because you have to know exactly how long each generation is. But new studies done by Linda Vigilant and her team – a number of primatologists in Germany – have studied the actual generation times using DNA and observations in the field of chimpanzees and gorillas, and we know them in modern humans. What this comes out to is about half the rate that researchers have been using for the past 15 years. One study by David Reich at Harvard and his colleagues comes up with a slower rate, but it isn't half the rate. And that raises some questions about whether the new genome methods are actually catching all the mutations. We're sort of at the limits of their resolution. I think most geneticists think that the rate is definitely slower. There is still some debate about precisely how much slower. Is it half or a little bit less?

Interviewer – Edward Hurme
When researchers are looking at the average, is it possible that there are times when mutation rate is faster or slower, or is the average a good estimate of what might be happening over many, many generations or millions of years?

Interviewee – Ann Gibbons
This new mutation rate is probably an accurate reflection of what the actual mutation rate is in living humans. Most researchers feel like they're in the right ballpark now for that. They get into trouble, though, when they try to extrapolate it back in time, because we don't know all the factors that could have slowed down or sped up the mutation rate over the past five, six, seven, ten million years. So, some examples of the things that can alter that rate are variation in generation time. Maybe our ancestors had shorter generations on average. Would that speed up the clock? Or maybe they had longer generations on average with polygamy and different kinds of social systems. Fathers could have been quite old when they had several wives, so maybe the mutation rate was longer and that would slow down the clock. Another factor is the age of fathers at conception. A new study by Kong and his colleagues that was published in August found that the older the father, the more mutations their children had. So you can see it's a little bit hard to extrapolate it back. Another factor is did our early human ancestors, Australopithecines,

for example, grow up faster and had their children younger? So that would affect the rate. And then finally, we don't know what the rate is precisely in chimpanzees or gorillas, and we're assuming their rate is the same as ours when we date events in human evolution. So now it's really important for researchers to go out. This work is being done to actually calculate the exact rate in chimpanzees today, and the exact rate in gorillas. Again, of course, we have trouble extrapolating those rates back to the ancestral gorillas or chimpanzees, because things like population size can affect the mutation rate. If you have a large population, the mutation rate is slower than in a small population.

Interviewer – Edward Hurme
So can you give us an example of some of the new dates for human evolutionary events?

Interviewee – Ann Gibbons
Yes. So if you apply the new mutation rate, you get a human-chimpanzee split of about 8.3 million to about 10.1 million years ago, instead of 4-7 million years ago. So that's quite a bit older. And the earliest fossils of the human family only are about 6-7 million years, so there's a problem there. The human-Neandertal split used to be 250,000 to 350,000 years ago. Now it's about 400-600 thousand years ago. That fits with fossils that look like they're ancestral to Neandertals that show up around 500,000 years ago in Europe. So that's a little better fit. And finally, we date the out-of-Africa migration to earlier, that we have our modern human ancestors coming out of Africa 90,000-130,000 years ago instead of less than 60,000 years ago. That would mean some of the fossils that have been discounted as modern human ancestors – especially in North Africa and Arabia – might actually be ancestral to modern humans if that's accurate. There will be some debate. I would say at this point anthropologists and paleogeneticists who use these dates are quite confused, and they're taking a wait-and-see attitude to see what geneticists end up deciding about applying these dates back in time.

Interviewer – Edward Hurme
Well, Ann Gibbons, thanks for talking with me.

Interviewee – Ann Gibbons
You're very welcome. Thank you.

Host – Sarah Crespi
Science News contributing correspondent Ann Gibbons writes about new evidence of a slower molecular clock in humans this week.

Music

[23:48]
Host – Kerry Klein
If you're a researcher and you're ready to get published, which journal do you target? Where do you turn if you've been rejected? Do revisions improve your paper? The answers for the questions vary for every researcher, and yet, according to Vincent Calcagno, publishing patterns do exist. Calcagno spoke with me about what he calls "the

science of science-making," beginning with how he became interested in such an unusual area of study.

Interviewee – Vincent Calcagno
Originally, being an evolutionary biologist, I had no specific interest in that. But as many researchers, I guess, I got frustration of having a piece of research I liked very much, and I got rejected several times in a row by different journals. And as many researchers, I got interested in how often does this happen? Is it common? What are the implications? Do we really lose time? And can something be improved about that? And I realized that we knew almost nothing about that. All that the evidence that we had were very fragmentary. So I decided to carry out a large-scale and systematic study of this flows of manuscripts.

Interviewer – Kerry Klein
And large-scale, indeed, it was. You had a tremendous amount of data. So tell me, you know, what was the data that you collected, and how did you get it?

Interviewee – Vincent Calcagno
Yeah. I tried to cover a broad spectrum of fields. So we make a selection of about 16 fields, ranging from genetics, ground science, ecology, evolutionary biology, trying to keep them consistent. And we sampled old journals that were categorized in those 16 categories, so that's about a thousand different scientific journals. And we studied all articles that they had published for three years, between 2006 and 2008, and so that represents about 200,000 articles for which we tried to retrieve the submission history.

Interviewer – Kerry Klein
And so you then obtained all of the specific data by writing a computer program that could present each corresponding author with a questionnaire about, you know, the particulars of their submission process. So once you had all of this data from tens of thousands of articles, what sorts of patterns were you looking for?

Interviewee – Vincent Calcagno
The first thing we were able to with all this data is connect all the journals together and build what we call often a map of science. So we were able to determine which journals were exchanging articles with other journals. So we were able to build a big network that represents the proximity of different journals and the intensity at which different journals exchange research manuscripts. And from this, what I call the hidden map of science, because it relies on data that has been so far hidden from public knowledge, we were able to look at different things. For instance, we found a strong role of the impact factor of journals shaping the submission strategies. And we were also able to show that the history of submission of articles had movements on their citation type, so the impact they had, in terms of citation count following that publication. And we also, we like, looked at different things. But how well can impact factor explain the importance of a journal in this submission network, and so how much does it correlate with impact it has on citation patterns as we usually use?

Interviewer – Kerry Klein
Well, let's start with impact. So what sort of role does a journal's impact factor play in its pattern of submissions and resubmissions?

Interviewee – Vincent Calcagno
So we found a sign that most central journals – the ones that are connected to many, many different journals in the network – were also the one that had high impact factor, as we could expect. So submission flows tend to follow impact factor in a way. And then we dissected this correlation to look at more specific impacts that impact factor could have on submission strategies. And we found that at resubmission, researchers systematically went down on the ranking of impact factors. So they tended to try first high-impact journals and then go to lower-impact journals. And this pattern was very strong. There is a strong bias in the resubmission flow, as we could expect. And we also found more surprising results. For instance, high-impact factors were also the ones that were publishing the fewer first-intent manuscript, as we call them. So a first-intent manuscript is a manuscript that was first targeted at the journals. So low-impact journals published mostly articles that were directly targeted at them, whereas high-impact journals frequently recycled manuscripts from other journals and published more articles that are, in fact, resubmissions from another journal, which is not what we expected.

Interviewer – Kerry Klein
Right, indeed, because as you said, the flow of resubmissions sort of only goes in one direction, that usually the first submissions are at the high-impact journals and then they go down the line if they're rejected.

Interviewee – Vincent Calcagno
Yeah. This sounds a bit paradoxical maybe.

Interviewer – Kerry Klein
Yup. And let's have some numbers. I mean, of all of the manuscripts submitted to publications, how many of them are actually published on first-intent?

Interviewee – Vincent Calcagno
Yup, that's really interesting too. Overall, we were surprised to find that about three-quarters – 75% - of all articles published in those journals had been initially submitted to the journal that would publish them. So as a scientist, I had an expectation that this would be higher from my personal experience and maybe with my colleagues, the same. So it was difficult to know what we would find. And in fact, most articles seemed to be first targeted at the correct journal – the right one, if you wish, because it will be published there, possibly after many revisions.

Interviewer – Kerry Klein
So many researchers have the right sort of risk in mind, and they hold their papers in the correct esteem to get it published the first time.

Interviewee – Vincent Calcagno

Yeah, I would take this as the ability and the knowledge of scientists in optimizing where they target their research to minimize the time and the effort they would lose being rejected.

Interviewer – Kerry Klein
And then you mentioned that you also studied citation history of various papers that are published. Did you notice any correlations between those that were published on first-intent and those that were published after resubmitting?

Interviewee – Vincent Calcagno
Yes, we did. So having been able to discriminate between articles that were first-intent and articles that were resubmission, we downloaded the citation data about three years after the publication of all those articles and compare the number of citations they received depending on their submission history. And we found that, surprisingly for us, while we'd not expecting trends, that resubmissions, or articles that had been published and previously rejected by another journal, were more cited than first-intent publications. And this is whether it is controlling for the year of publication and the journal.

Interviewer – Kerry Klein
Wow! What do you think could be the reason for that?

Interviewee – Vincent Calcagno
There could be several mechanisms that contribute to that pattern, and it will be interesting to find out exactly what's happening. But the most likely explanation that we have is that just spending time reviewing journals, maybe this improves intrinsic quality of the final product, the article that gets published. And so maybe those articles that have undergone a long submission process, being rejected in the end were slightly better than the ones that had directly been accepted in the journals. And we think that's a more likely explanation, because we did not find any difference between resubmissions that came from lower-impact journals and those that came from higher-impact journals. So we don't think this reveals the intrinsic potential quality of the results, but rather the benefits of having been more reviewed and edited by different peers.

Interviewer – Kerry Klein
Wow, how interesting. Well, so then do you have any advice for a researcher who is soon to be publishing and looking to make the highest impact in their field of research?

Interviewee – Vincent Calcagno
Yes, that's what many people ask me. I don't think there's a magical recipe that we can have. But if we are to integrate our results in that direction and try to have some guidelines, the advice will be we should try the big journals – try the big ones. So don't really think, "Oh, maybe I'm going to lose a lot of time and spend a lot of effort trying big journals, and in the end I will be rejected, and maybe I should go directly to a lower journal and get directly accepted." So, of course, trying and being rejected is a waste of time and very frustrating. But not everything is lost. Maybe this isn't the end; the final product maybe is better, and we will be more cited after publication, which is kind of

compensation for the frustration and the effort. And the other aspect is maybe about – I did not talk about that a lot – but there's an effect, too, of resubmitting across fields, or resubmitting within journals of the same field. And since we find that resubmissions occurring across fields are, incidentally, less cited following publication, my advice would be do not change radically the type of journal and the scientific community of the journals at resubmission because you will maybe lose a bit of impact. And the real reason for that will be interesting to find, but it suggests that we gain from staying within a community of journals to the resubmissions.

Interviewer – Kerry Klein
Right. Great. Well Vincent Calcagno, thank you so much.

Interviewee – Vincent Calcagno
It's been a pleasure.

Host – Kerry Klein
Vincent Calcagno and colleagues reveal the hidden patterns in scientific publishing in a paper published online this week. You can read the article at www.sciencexpress.org.

Music

[33:50]
Host – Sarah Crespi
In the brain, addictive drugs are generally understood to employ similar mechanisms to highjack similar reward systems. But in a Report published last week, Eric Nestler and colleagues describe a surprising discrepancy between how two families of drugs behave in the brain.

Interviewee – Eric J. Nestler
What we had shown previously, and other labs have done as well, is that cocaine and other stimulants seem to, over the long term, produce this feed-forward response, where the brain becomes more sensitive to the stimulants, partly through a molecule called BDNF, this growth factor that tends to promote nerve plasticity in the brain. What we found in this paper—somewhat surprisingly, given the fact that opiates and cocaine do converge in producing the same effect on dopamine pathways—is that they produce the opposite effect on this modulatory protein called BDNF.

Host – Sarah Crespi
That was a snippet from Eric Nestler's podcast interview with Annalisa VanHook on the *Science Signaling* podcast. You can hear the whole interview at stke.sciencemag.org.

Music

[35:01]
Interviewer – Edward Hurme

Finally today, I'm here with online news editor David Grimm, who's here to give us a rundown of some of the recent stories from our online daily news site. So David, in our first story we'll look at the first trial of using neural stem cells in children. So what exactly is this disease that these children were suffering from?

Interviewee – David Grimm
Well Edward, it's a very rare and fatal brain disease known as Pelizaeus-Merzbacher disease, if I'm saying that correctly. And basically this is a disease where people have a lot of trouble producing a protein called myelin. Myelin sort of forms this sheath around neurons, and it actually sort of insulates neurons and helps them transmit electrical signals between each other. And obviously that would be very important in children with this disease that lack this myelin because actually they have problems with cells called oligodendrocytes, which produce myelin. These children have a lot of trouble talking, walking, even breathing on their own, and they often die very prematurely. So what this new study is all about is trying to find a way, you know, with stem cells, can we somehow get myelin back into these kids? And researchers have actually been looking at this question for a long time. And what they've been trying to do is trying to find human stem cells that will generate these oligodendrocytes, which produce myelin. And they've done a lot of animal studies, and actually recently, they've isolated some stem cells that seem to really do the job well in mice. When they gave these stem cells to mice, 60-70% of the time, the cells became oligodendrocytes and began producing myelin.

Interviewer – Edward Hurme
So how do you actually go about treating this brain disease with stem cells? What did the researchers do to treat these boys?

Interviewee – David Grimm
Well so what they did, you know, moving from mice to kids was they actually drilled small holes in the children's skulls. And it sounds extreme, but these were actually small holes just sort of big enough to get a fine needle into there. And then they basically squirted millions of these stem cells into the white matter of the children's brains. And this was done on four boys with the disease. And then they monitored the boys for about a year. And they found that at the end of the year, all the boys showed changes in their brain that were consistent with more myelin. And they also didn't have any side effects. And that's actually one of the big things that these trials are trying to do: not necessarily prove efficacy at first – although that's ideal – but just to prove that a therapy is safe. And at least in this case, it seems to be safe. And as a bonus, they actually saw that the boys actually seemed to have modest improvements in their development. For example, a five-year-old boy in the study began, for the first time, to feed himself and to walk without assistance during the study. So that was a pretty encouraging sign.

Interviewer – Edward Hurme
So what does this mean for the future of stem cell therapies, and even neural stem cell therapies?

Interviewee – David Grimm

Well, it's a good question. It's not just this disease that these researchers are concerned about because obviously this is a very rare disease. But there's a lot of factors of this disease that overlap with diseases like Parkinson's disease and multiple sclerosis, which are far more common. So the hope is that if the researchers can really sort of nail down this technique and make it work for this particular disease, that it could be applied to diseases that are much more common but also have a lot of very devastating neurological effects.

Interviewer – Edward Hurme
So our next story looks at how models of the spread of a disease found an unlikely reservoir for a virus. And the virus in question is known as EEV. So what is EEV?

Interviewee – David Grimm
Well, it's actually – you forgot an E there, Edward. It's actually EEEV, and it stands for Eastern equine encephalitis virus. And this is a very devastating disease that primarily strikes horses and kills horses, but it can actually also infect humans. And almost 35-50% of humans with the disease die. So this is a really big problem. It seems to be prevalent along the eastern coast of the United States and tends to emerge as the weather gets warmer. And what scientists know is that EEEV is spread by mosquitoes. But there's a mystery because mosquitoes die in the winter, and that should really wipe out this virus. And yet every year the virus seems to come back. And that suggests to the scientists there must be what they call a reservoir. There must be another animal besides mosquitoes that's holding onto this virus so that the virus can reemerge back when the winter is over.

Interviewer – Edward Hurme
So how did the researchers figure out where this reservoir might lie?

Interviewee – David Grimm
Well, they had two prime suspects: either birds or reptiles. And they searched through a lot of the birds, and they found out that birds just rid themselves of the virus too quickly. When they get infected, they really get rid of it too quickly to be able to harbor it for months and months over the winter. So they didn't really seem like the likely reservoir. So they looked at a bunch of reptiles, and they also didn't see a lot of promising signs there until they looked at snakes. And specifically, they looked at several different species of snakes in Alabama's Tuskegee National Forest, and that's a place where EEEV is known to strike. And they tested the blood of the snakes, and what they found was that in two species of snakes, specifically the cottonmouth and the copperhead, more than 35% of the cottonmouths had antibodies against the virus, and 22% had bits of the virus's DNA in their blood. So this was a pretty strong indication that these cottonmouths – and probably the copperheads as well – are able to harbor this particular virus.

Interviewer – Edward Hurme
So how did they actually prove that the virus is staying in the snakes over the wintertime?

Interviewee – David Grimm

Well what they did was they actually brought some garter snakes back into the lab. They didn't want to use cottonmouths or copperheads because they didn't really want to get bit, so they chose garter snakes, which are nonvenomous. And they showed that in these garter snakes, the virus persisted even during the snake's hibernation, and it remained active even after 30 days of what they call cold-induced sleep. So this virus really stuck around in these animals, and it was still present at pretty high levels. And when I say virus, I don't actually mean virus. And that's actually one of the potential downsides of this study, because the researchers actually didn't find the virus itself. What they found was these antibodies and these bits of RNA that are related to the virus, and that's one possible downside. One expert said, you know, we can't really be conclusive about the snakes being the reservoir until we actually find the virus itself in these reptiles.

Interviewer – Edward Hurme
So from disease potentially hiding under the skin of snakes, our third story looks at a certain species of octopus that's hiding something under its skin as well. So, David, what can you tell me about the blue-ringed octopus?

Interviewee – David Grimm
Well Edward, this is a golf ball-sized octopus, and it's actually very poisonous – speaking of poisonous animals. It can actually kill an adult human within minutes. And what it does is actually bites people, or bites other animals, and releases venom through its beak – actually venomous saliva. But before it does this, it's kind enough to sort of give off a warning signal. And the warning signal is dramatic. It flashes these bright blue rings of light, and you can actually see a video of this on the site. And scientists have wondered how does this work? Where is this light coming from, and how actually are the octopi flashing them in the first place?

Interviewer – Edward Hurme
I'm guessing this is different from how octopuses normally control their colors.

Interviewee – David Grimm
You know, a lot of time what octopuses usually do is they activate what are called chromatophores, which are basically sacs of pigment. And these chromatophores give off color, give off light. And that's kind of what's happening here, but it's a little bit different. What the researchers found by dissecting a few of these octopi in the lab was they found that actually these blue rings of light are pretty much always on. But what happens is that they are actually concealed by pouches of skin normally. And what the octopi do is when they get agitated, they release one set of muscles and tense another set of muscles, and that basically just gets the pouches out of the way. You can almost think of it like a spotlight that's always on, but it's sort of got a cover on it. And when the octopi flex their muscles, they're basically removing that cover, and the light shines through again. And that's sort of what's happening.

Interviewer – Edward Hurme
And David, what else have we had on the site this week?

Interviewee – David Grimm
Well Edward, for *Science*NOW, we've got a story about how mites seek revenge on their childhood foes. Also, a story about how a feast of ribs shedding light on early human behavior. For *Science*Insider, we've got a story about the controversy over genetically modified crops in India. Also about how President Obama and Governor Mitt Romney differ on energy policy. And finally, for *Science*Live, our weekly chat on the hottest topics in science, this week's *Science*Live is all about new therapies for mental illness, and it actually will have already taken place by the time this Podcast comes out, but you can check out a transcript of the chat on the site. Next week's chat is going to be about the Nobel Prizes. Do the Nobels need an overhaul? And just one more thing to note. We are running our annual Dance Your Ph.D. contest. This is a contest for scientists who can interpret their Ph.D. theses in dance form. We have collected all of the entries for this year. And the 12 finalists have been picked, and you can go on our site to check out the 12 finalists in four different categories and vote for your favorites. We'll be announcing the winner next week. So be sure to check out all of these stories on the site.

Interviewer – Edward Hurme
Well David, thanks for talking with me.

Interviewee – David Grimm
Thanks, Edward.

Interviewer – Edward Hurme
David Grimm is the online news editor of *Science*. You can check out all our news at news.sciencemag.org, including daily stories from *Science*NOW, and science policy from *Science*Insider. While you're there, be sure to check out *Science*Live, a live chat on the hottest science topics every Thursday at 3 p.m. U.S. Eastern time.

Music

Host – Kerry Klein
And that concludes the October 12th, 2012, edition of the *Science* Podcast.

Host – Sarah Crespi
If you have any comments or suggestions for the show, please write us at sciencepodcast@aaas.org.

Host – Kerry Klein
The show is a production of *Science* Magazine. Jeffrey Cook composed the music. I'm Kerry Klein.

Host – Sarah Crespi
And I'm Sarah Crespi. On behalf of *Science* Magazine and its publisher, AAAS, thanks for joining us.

Music ends