Editors' note: The document below compares Helen Pearson's submitted draft of her profile of evolutionary biologist Joe Thornton with the final, published version of the story.

~~Hed: The future of the past// Resurrection lab//~~Prehistoric proteins: Raising the ~~molecular~~ dead~~// The evolutionary activist// or other~~

~~Dek:~~To dissect evolution, Joe Thornton resurrects proteins that have been extinct for many millions of years ~~in an effort to dissect evolution. And he's fought some surprising battles on the way. [or something about his activism for G/peace~~. His findings rebut creationists and ~~intelligent design]]~~challenge polluters.

Halfway through breakfast, Joe Thornton gets a call from his freezer.

A local power cut has triggered an alarm on the ~~-80ºC lab~~ −80 °C appliance in his lab at the University of Oregon~~,~~ in Eugene, and it has sent out an automatic call. Thornton breaks off ~~the~~our conversation and calls his senior research scientist, Jamie Bridgham, to make sure that the back-up generator has kicked in. If the freezer starts warming up, a lot could be lost — not least a ~~vast~~valuable collection of proteins that ~~were~~had been extinct for hundreds of millions of years until Thornton and his team ~~resurrected~~brought them back from the dead.

~~Amongst that collection is~~One deep-frozen vial holds the more-than-600-~~800~~-million-year-old ancestor of ~~a receptor family~~the receptors for oestrogen, cortisol and other hormones, which Thornton brought to life ~~in 2003~~ [ref 1]~~; and the 400-450 million year old~~ nine years ago. Other tubes house proteins ~~that he~~ more than 400 million years old, which Thornton resurrected a few years later ~~in a feat of molecular reconstruction that revealed~~to show how an ancient receptor had changed its preferences — and how the march of evolution ~~had run forwards but could not play back~~ [2,3,4]~~. It also contains~~cannot be reversed. In another corner of the freezer rest the ancient protein components of a sophisticated cellular machine that~~, his group showed in *Nature* this January, evolved from a simple to~~ acquired a more complex form through ~~the~~ random ~~accumulation of~~ mutations rather than ~~because~~ selection ~~drove it towards a~~for superior ~~machine~~ [5]~~.~~function, as the group showed in *Nature* this January. The sheer awe of working with long-dead proteins ~~doesn't~~doesn't fade, ~~he~~ says~~. "It's~~ Thornton. "It's amazing. The ability to do this type of time travel is fantastic."

~~The work has made~~
Thornton is a leader in a ~~field that he has called a 'functional synthesis' between the theories of evolutionary biology and the sophisticated experimental tools that pick molecules apart~~ [6, Nature reviews]~~.~~movement to do for proteins what the scientists in *Jurassic Park* did for dinosaurs: bring ancient forms back to life, so that they can be studied in the flesh. "Instead of passively observing things as most ~~of~~ evolutionary biologists do, you actively go in and test the hypotheses experimentally," says Antony Dean ~~who leads another major group in the field at~~, a molecular biologist at the University of Minnesota~~,~~ in St Paul~~. "He's~~ who heads another major group in the field. "His is one of the leading labs, no doubt." And ~~he's~~Thornton is tackling some

important questions, says Kenneth ~~R.~~ Miller ~~[he wants the R in name],~~ a molecular biologist at Brown University in Providence, Rhode Island. "~~He's~~He's helping to put some flesh on the bones of speculation about how complexity arises."

What ~~isn't~~isn't so widely known is that evolutionary biology is ~~Thornton's~~Thornton's second career: in his first, he was an activist for Greenpeace, campaigning vigorously against the release of toxic chemicals. He wrote a ~~well-received~~controversial book on organochlorines~~,~~: industrial chemicals that include dioxins, polychlorinated biphenyls (PCBs~~, DDT~~) and ~~other~~ pesticides such as DDT. That activist legacy bleeds into his work today~~. For~~, for example in his ~~main system of study, he chose the steroid hormone receptors, a family that includes~~focus on the oestrogen receptor, which is corrupted by many ~~chemical~~ pollutants. The grubby, sea-green tiles under ~~Thornton's~~Thornton's lab benches were carefully sourced to be free of ~~poly vinyl~~polyvinyl chloride (PVC), one of the ~~organochlorine~~organochlorines that worries him ~~the~~ most. ~~The experience~~ His activist past also ~~means~~helps to explain why he has been fearless — almost enthusiastic — about highlighting the challenge that his work presents to ~~proponents of~~a creationist argument called intelligent design~~. Their claims~~: the claim that complex molecular systems can only have been created by a divine force ~~are crushed by his experiments showing~~. Thornton shows how evolution ~~can do the creating~~did the job, leaving no need for a designer.

~~His activist past also, Thornton says, colours the way he views the scientific process as a whole — not as one of pure discovery, but one in which scientist's claims are inevitably shaped by their cultural viewpoint, biases and agendas. "It makes me want people to identify their presumptions — and it may make me question presumptions that others might take for granted," he says.~~

~~Break~~

~~Thornton's~~Environment to evolution

Thornton says that his activist days — during which he saw that many risk-assessment models were shot through with assumptions and biases — left him "intensely committed to methodological reductionism and experimentalism", which he now uses to break evolution down into detailed steps that he can test. "If you're doing science, I think it ought to be as strong and decisive as possible," he says. "If you're doing politics, go ahead, but don't try to disguise it as science."

Thornton's unconventional ~~route into science~~career path started ~~in the suburbs of Chicago, where~~with an obsession with ~~*Moby Dick*~~, which led him to study English at Yale University in New Haven, Connecticut. But the course, with its focus on the philosophy of criticism rather than literary texts, left him with a hunger for reality, and nothing seemed more real than politics and activism. He dropped out of college, signed up with Greenpeace and spent several months ~~doorstepping to canvass people for money and support. The experience, in which "you have to engage people in about 5 seconds and get some compelling argument across in maybe 30 seconds", taught him a lot about framing arguments for the varying audiences he encountered in neighbourhoods ranging from affluent to working class.~~

~~By~~doorstepping to canvass people for money and support.

In the early 90s, Thornton was becoming more involved in Greenpeace's campaigns to build community opposition to 1990s, Greenpeace was campaigning against sources of toxic pollution, a growing national issue at the timeand Thornton was drawn in. He became the "science guy", reading the scientific literatures and 'science guy', translating itthe scientific literature into reports and other material that communities and Greenpeace could use to make their case. "I spent a lot of time analysing [industry] risk assessments and ripping their logic and assumptions to shreds," he says. [OR IYou could rely on Joe when you didn't have quotes from thoseenough knowledge of an issue," says Charlie Cray, a research specialist at Greenpeace in Washington DC, who worked with him then]Thornton. His reports "put a challenge out there that industry couldn't answer". One campaign hethat Thornton helped organiseto organize, against plans to build more than 100 hazardous -waste incinerators nationwideacross the United States, climaxed in May 1993 when Greenpeace parked a truck dressed up as an incinerator outside the White House and some 60 people chained themselves to concrete blocks.it. The next day, the Environmental Protection Agency announced a moratorium on new hazardous waste incinerators [http://www.nytimes.com/1993/05/18/us/administration-to-freeze-growth-of-hazardous-waste-incinerators.html?pagewanted=all&src=pm].

But Thornton says it wasn't lack of progress that drove him out of activism — it was growing older, and wantingyearning to "develop my own body of work."". His time with Greenpeace had madetaught him aware of the power of science to influence science can have in society, and he wanted to join that influential world. But firsthis ambitions turned to research. First, he had to deal with the small matter of graduating from Yale. By this point Then living in New York, he did that by accruing course credits at Columbia University — attending his first molecular--biology classes aged 30 [chk] — only to find himself rejected from almost every graduate schoolprogramme he applied to for, in part because of his unusual resuméCV.

Break

Of the seven friends and colleagues of Thornton's that I interviewed before meeting himThornton's who spoke to *Nature*, six called him intense. The seventh described him as "beyond intense". But only a little of that intensity is apparent at his Wednesday morning lab meeting in Eugene. The freezer crisis has blown over by now: the power came back after half an hour and the thermometer rose to only hit -76ºC−76 °C. Now graduate student Dave Anderson gets a friendly grilling during a practisepractice talk outlining his thesis proposal: to trace the evolution of the DNA-binding domain of an ancient hormone receptor. The meeting stretches on for 2.5 hours — not uncommon for a Thorntonin this lab meeting, everyone says.

A binding fascination

Since his Greenpeace days, Thornton wrote in his graduate school application essay that he wanted to study the evolution of molecular complexity through has been fascinated by the steroid hormone receptors, a family of six receptors,: in vertebrates, six proteins that sit in the cell nucleus and control the activity of other genes. The interest stemmed directly from his Greenpeace work, he says, which showed him that by By binding specific 'ligands''ligands' — hormones ranging from oestrogens toand

androgens to cortisol — the ~~receptor family triggers~~receptors trigger "these remarkable cascades of biological activity during development and physiology~~"~~", Thornton says. "Their affinity for their hormones is just stunning. A drop of hormone in a railroad tank car of serum is enough" — and yet, as Thornton learned at Greenpeace, they can be waylaid by toxic substances. ~~[chking if this true of other receptors besides oestrogen]~~ "I wanted to know where that system came from," he says.

When ~~Columbia University~~he was finally accepted ~~him~~ for ~~his~~a PhD at Columbia, he set about ~~piecing~~comparing receptor genes from living organisms to piece together ~~from gene sequences~~ a detailed history of how the receptor family had evolved ~~[6 PNAS].~~.

Just as ~~he~~Thornton completed his first year of ~~grad school, though~~graduate study, however, MIT Press called~~. Would~~ to ask if he would write a book on organochlorine pollution~~?~~. He ~~would and he did, working~~worked in the lab during the day and ~~writing the book~~wrote at night ~~from~~, in a tiny room in his Brooklyn apartment, encircled by towers of papers that eventually formed the nearly ~~1200~~1,200 references and ~~599~~611 pages ~~in *Pandora's*~~of *Pandora's Poison*~~.~~, which came out in 2000. "I was shocked when I saw the book," says Rob ~~Desalle~~DeSalle, who studies molecular evolution at the American Museum of Natural History~~,~~ in New York, and co-supervised ~~Thornton's~~Thornton's PhD. ~~"~~He ~~could've~~could've been writing~~"~~ *War and Peace*~~"~~ and I ~~wouldn't~~wouldn't have known it."

The book~~, when it came out in 2000,~~ caused a ~~wider~~ stir. Drawing on arguments ~~Thornton~~that he had formulated ~~during his later days~~ at Greenpeace, ~~he argued~~Thornton made the case that regulatory policy should focus on managing classes of toxic chemicals ~~—~~—rather than tens of thousands of ~~individual~~ substances, one by one — and that the priority should be organochlorines~~, a vast group of particularly persistent toxins~~. These substances, generated by the use of chlorine gas~~. Thornton says that representatives of~~ in the chemical and paper-making industries, have properties of stability and solubility that make them desirable to industry ~~fought back: certainly, Amazon reviews either applaud or slam the book with little in between [[Thornton says~~ but problematic to the ~~stinging reviews were written by reps of the chemical industry; one~~ environment because they are long-lived and accumulate in animal tissues. *Nature*'s review ~~can be traced to someone at the~~ called *Pandora's Poison* a "landmark" and another review compared it to Rachel Carson's famous 1962 treatise on pollutants, *Silent Spring*. The Chlorine Chemistry Council ~~but would take more work to confirm this]].~~ in Washington DC, however, decried Thornton's "hyperbole and faulty risk analysis".

But Thornton was already gearing up to make a different kind of splash, ~~this time~~ with his first paper in *Science* ~~paper in 2003.~~[1]. He and his team trampled the assumption that only vertebrates have steroid hormone receptors ~~were only present in vertebrates~~ by cloning one from the sea slug ~~(~~ *Aplysia californica*~~) and revealing~~. The finding implied that the origin of the receptor gene was far more ancient than anyone had ~~realised [1, Science 2003].~~realized. "I ~~would've~~would've hated to be a fellow grad student~~, he~~. He was writing a book and publishing in~~"~~ *Science*~~"~~ and having two children at the same time," says Darcy Kelley, a ~~TK~~biologist at Columbia ~~University,~~ and ~~his~~Thornton's other PhD co-supervisor.

The approach that Thornton took in the 2003 study is one that he has loosely followed ever since. ~~Based on~~Starting with the ~~gene sequences of~~genes for steroid hormone receptors from a slew of ~~diverse~~ living organisms, he clambered backwards through the evolutionary tree to deduce the most likely sequence of the common ancestor of all such receptors, which existed some 600~~-~~ million to 800 million years ago ~~[[~~, in the common ancestor of "you and a snail~~""~~", as he puts it~~]]. Then, at the point where~~. Instead of stopping there, as most evolutionary biologists ~~had conventionally stopped~~would have done, he then built the gene and inserted it into cells that could manufacture the ancient protein.

~~Once brought to life,~~
Resurrecting the protein, says Thornton, allowed his team ~~showed~~"to experimentally test hypotheses about evolution that ~~the~~would otherwise be just speculation". They went on to show[1] that the ancestral receptor was sensitive to oestrogens but not ~~other~~to related ~~steroid~~ hormones — supporting the idea that the family of receptors evolved through a series of gene duplications and that the copies gradually evolved ~~an affinity for other ligands such as progesterone and testosterone. [[The appeal of the method, says Thornton, is "the ability to experimentally test hypotheses about evolution that would otherwise be just speculation."]]~~affinities for other ligands.

~~Break~~

By the time his ~~*Science*~~ paper came out in *Science*, Thornton had taken a faculty position ~~at~~in Eugene, an old hippy town ~~which~~that pays as much homage to bicycles as it does to cars. He built a house (no PVC, sustainable bamboo floors~~),~~) and set to work building up his protein ~~-~~-resurrection lab.

~~He~~Thornton wanted to delve deeper into the puzzle of how complex systems ~~—ones~~ with tightly interacting molecular parts ~~—~~evolve. It was a ~~longstanding~~long-standing conundrum. As Charles Darwin wrote in *On the Origin of Species*~~,~~: "If it could be demonstrated that any complex organ existed which could not possibly have been formed by numerous, successive, slight modifications, my theory would absolutely break down~~".~~." And what was an evolutionary puzzle to biologists was a target for ~~creationists~~evolution's critics. Michael Behe, a biochemist at Lehigh University in Bethlehem, Pennsylvania, and a senior fellow at the ~~creationist~~ Discovery Institute ~~[chk]~~in Seattle, Washington, proposed in the 1990s that such systems — the ~~eye~~blood-clotting cascade, for example, or the molecular motor called the flagellum ~~——~~— are so "irreducibly complex" that they could not have evolved step by step, and can only be the product of intelligent design.

Thornton says that he ~~didn't choose~~didn't set out to ~~tackle the evolution of complex systems because the results could~~ refute intelligent design, but the prospect of a fight hardly put him off. "Been there, enjoyed that," he says. He chose to explore ~~the complexity encoded in~~ a pair of steroid hormone receptors: the mineralocorticoid receptor (MR), which binds the hormone aldosterone and regulates salt and water balance~~,~~; and the closely~~-~~ related glucocorticoid receptor (GR~~)~~), which binds cortisol and controls stress response. A gene duplication ~~some~~more than 450 million years ago produced the two receptors — but aldosterone ~~didn't~~didn't arise until ~~much~~many millions of years later. The ~~puzzle was,~~timing seemed to make the MR a textbook

example of irreducible complexity: how could selection drive the evolution of a lock (the MR) to fit a key (aldosterone) that ~~didn't even~~didn't yet exist~~; equally, how could selection sculpt a key for a lock that wouldn't accept it? ~~ ?

Evolution at work

Led by Bridgham, ~~Thornton's~~Thornton's team found the answer by resurrecting the ~~450 million year old~~ ancestor of both receptors. To their surprise, ~~the ancient receptor~~it was sensitive to aldosterone, suggesting that it had been activated by an ancient ligand with a similar structure~~ [2].~~[2]. Once aldosterone had evolved~~ many millions of years later~~, the team proposed, evolution was able to take advantage of the existing receptor to control a new biological ~~functions~~function — a process that Thornton termed ~~'~~molecular ~~exploitation'.~~ exploitation. They also showed how its sister receptor, the GR, was evolving functions of its own.

"Such studies solidly refute all parts of the intelligent design ~~hypothesis~~argument," wrote ~~Christopher~~Christoph Adami~~ of~~, an evolutionary biologist at the Keck Graduate Institute of Applied Life Sciences in Claremont, California, in an ~~accompanying perspective~~ article ~~[Science 312, 61-62 (2006)].~~entitled 'Reducible complexity'. But Behe~~, in a post on the Discovery Institute website,~~ dismissed the result. ~~"~~The ~~isolated components they work on~~receptor and ligand are not irreducibly complex~~," he wrote. [http://www.discovery.org/a/3405]~~ **~~[TK – interview~~**, he says, and evolution did not give them any truly new function. "I think his results are quite consistent with **~~Behe]~~** my own view that Darwinian processes are poor ones to explain the complexity found in life," Behe told *Nature*.

Thornton ~~began to subject his resurrected proteins to~~turned up more ~~sophisticated biochemical analyses. This time,~~ clues to the workings of evolution when his team explored ~~how~~ the ~~other copy~~history of the ~~receptor~~GR, which became sensitive only to cortisol over ~~some 40~~the course of about 20 million years~~ [chk], by identifying mutations that occurred during that period~~. Working with structural ~~biologist Eric Ortlund~~biologists at the University of North Carolina, Chapel Hill, the group determined the crystal structure of the ~~450 million year old~~common ancestor of the GR and MR.~~ They showed~~ They showed[3] that two ~~critical~~crucial mutations together altered the binding pocket of the ancestral receptor so that it ~~specifically bound~~preferred to bind cortisol — and identified another five ~~'permissive'~~ mutations that ~~were of little consequence on their own but nevertheless essential for setting the stage, by stabilising the protein so that it could tolerate the functional shift.[3]~~ finished the job.

In a final chapter to the story, Thornton tried to run that evolutionary sequence ~~in reverse. After all, the group knew that~~backwards. But when the researchers reversed the seven mutations~~, played forward, could turn a receptor sensitive to mineralocorticoids into one sensitive only to cortisol. But when they reintroduced the 7 mutations into the~~ in the ancient cortisol-specific form, they could not transform it back~~. [4, Nature 2009]. That's~~ into a protein that worked like the common ancestor of the GR and MR. They instead engineered a dud, unable to respond to any hormone[4]. That was because ~~of~~ a handful of other mutations ~~that~~ had also cropped up on the way to making a cortisol-specific receptor. They played little part in the ~~protein, but had~~

~~little direct effect on how it worked.~~ receptor's new function, but acted as an evolutionary ratchet, preventing it from regaining its old one.

Thornton showed that it was necessary to ~~reintroduce~~undo those mutations too, ~~in order~~ to reverse the change. ~~[not sure I have explained this clearly enough?!]~~ To ~~Thornton, it~~him, the work was a powerful demonstration that the path of evolution can be contingent on random events ~~of the past~~. “Chance plays a very large role in determining what evolutionary outcomes are possible,” he says. ~~[[OR “Our biology is one of many possible rolls of the evolutionary dice” he says.~~ The study captivated the scientific press — and beyond. “Evolution opens gateways into the future. But it appears to close them — firmly — behind it as well,” read ~~a leader~~an editorial in the *New York Times*. ~~[http://www.nytimes.com/2009/10/07/opinion/07wed4.html]]]~~

~~Break~~

In ~~his~~the Nature ~~study earlier~~article that was published this year~~,~~[5], Thornton took a break from ~~the~~ hormone receptors, and instead ~~collaborating~~collaborated with Tom Stevens ~~[chk],~~ a geneticist at Eugene, to dissect the evolution of V-ATPase, a molecular machine ~~called a V-ATPase which~~that pumps protons ~~into yeast~~across membranes to acidify compartments inside cells. The group wanted to know how an essential part of the machine — a ring of proteins that spans cell membranes — evolved ~~to contain three types of component~~ from an ~~earlier~~ancestral form ~~made up of~~with two components to one with three.

With their protein ~~-~~-resurrection toolbox, the researchers showed that, around 800 million years ago, the ancestral gene coding for one protein component was duplicated, and the daughter genes then picked up two vital mutations. ~~This~~The changes meant ~~it~~ that the proteins could no longer sit anywhere in the ring, ~~and~~but instead had to occupy a specific spot. Suddenly, the ring could ~~no longer~~ function ~~without~~only with all ~~3~~three parts. What surprised Thornton ~~the most~~ was that the ~~3~~three-component ring ~~appeared~~seemed to work no better than its ~~2~~ two-component counterpart~~: increased complexity arose through the random acquisition of~~. Random mutations ~~— ones~~ that actually corrupted ~~a protein — rather than those driven by selection.~~ proteins had led to 'irreducible complexity'.

Computing complexity

The ~~paper this year was~~study flipped another ~~flipped~~ finger to intelligent ~~-~~-design ~~propnents~~proponents — but “~~I’m~~I'm sort of bored with them~~,~~””, Thornton says. ~~He’s~~He is more excited by the next scientific story ~~that’s~~that is about to come out of the lab. ~~The~~His group wanted to explore how the ~~original 600-800 year old ancestral~~ancestor of the entire steroid hormone receptor family, which was sensitive only to ~~oestrogen~~oestrogens, evolved into ~~one that was~~forms sensitive to other hormones. And this time, he found no clues in the crystal ~~structure~~structures of ~~the~~ resurrected proteins from before and after the ~~mutations that drove this~~ change ~~offered no clue.~~ .

The answer can be found on a computer screen at the end of ~~Thornton’s~~Thornton's lab. Mike Harms, a ~~post doc~~postdoc who joined the lab three years ago, used his expertise in biophysics and some immense computational power to simulate the

~~movement~~movements of every atom in the ancestral receptors~~.~~, showing how just two mutations drove the transformation. When Harms hits play, ~~the 600-800 million year old receptor shimmies, and the~~an oestrogen molecule snuggles its way into the binding pocket of a receptor roughly 550 million years old. But when he runs a simulation of ~~a younger, [x million year old]~~the same receptor ~~runs~~with those two mutations, the oestrogen ~~molecule~~ never finds a comfortable spot ~~and water molecules stack up awkwardly on the outside. This type of modelling revealed that the younger protein could not form the right hydrogen bonding with oestrogen, so that it could no longer bind. [paper in review].~~

~~And there is another, poignant side to the~~ This evolutionary story also sheds light on why the oestrogen ~~receptor's history. [[During evolution, the~~ receptor is now vulnerable to the threats against which Thornton campaigned in his former life. The team worked out~~,~~ that each steroid receptor ~~is~~ evolved to be only as specific as it ~~has~~had to be to bind its target ligand and exclude all others that existed at the time. ~~]]~~ The oestrogen receptor achieves this by binding substances that ~~have~~contain a ~~specific~~ chemical structure called an ~~aromatised~~aromatized A ring. Because oestrogens are the only steroid hormones ~~[chk more than one oestrogen]~~ to have such a ring, that criterion was enough to ensure that the receptor ~~only~~ bound only oestrogens for many millions of years. Until, that is, the chemical industry started pumping out hundreds of substances ~~with aromatised~~containing such aromatized rings ~~that~~, which the oestrogen receptor unwittingly bound. "The endocrine ~~disruptors~~disrupters are taking advantage, unfortunately, of the promiscuity that is the result of the evolutionary history of receptors," Thornton says.

~~The latest result does not have any direct implications for how endocrine disruptors should be regulated — "but I don't think we need any more science to know what we need to do,"~~ Thornton ~~says. And he~~ does see progress on the issues on which he once campaigned. ~~He points to a reduction in production~~Production of toxic chemicals in the United States has fallen since his days with Greenpeace, and ~~the 2006~~in 2007 the European Union enacted REACH ~~[(~~Registration, Evaluation, Authorisation and Restriction of Chemicals~~] treaty in the European Union,~~), which ~~emphasises~~emphasizes elimination of the most dangerous substances ~~and~~. That law puts the onus on the chemical industry to show that a chemical is safe rather than on regulators to prove it is dangerous~~.~~ — the approach for which Thornton argued in*Pandora's Poison*.

Does he miss having something to campaign against? Yes and no. "~~I'm~~I'm less able to convince myself that the world has to be exactly as I envision it. So ~~it's~~it's harder for me to occupy that activist persona." Besides, he says, "My kids take all that energy now."

~~Later, back~~Or almost. His creations need tending too. Back in his office, ~~Thornton says he's glad to see more labs adopting the functional synthesis — more than 20 worldwide, he estimates. [[or better transition…]] Then~~ we listen to the tinny voicemail message left by the freezer on his phone earlier that day.

"The past is calling," Thornton says.

~~<<ends>>~~

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~~Box/graphic/explanation?~~

~~Vertebrate genomes contain six receptors for steroid hormones: two are sensitive to estrogens (ER); one is sensitive to androgens (AR), progestins (PR), glucocorticoids (GR) and minerlaocorticoids (MR).~~

~~Overmatter~~
~~At school he was also a member of the debating society: "which is a crazy activity where people become obsessed with gathering evidence — which is basically what scientists do except don't get evidence from library, get their evidence from doing expts." He also avidly played music, the bass, in a super intense rock band that practised 3 hours every day. "We were very intense. We were the most disciplined high school rock band I've even seen"~~

~~[[OR "It's sort of like the astronomers who can listen to the echoes of the big bang — except we can use those echoes to physically reconstruct the state of things in the deep past and then manipulate it."]]~~

~~(Thornton's children were also enjoying bottles and cups free of bisphenol A, long before most people had heard the chemical's name.)~~

~~This paper, and another by Steven Benner http://www.nature.com/nature/journal/v425/n6955/abs/nature01977.html] "marked the modern era of ancestral [something]," Thornton says. [better from another source~~

~~Thornton's hawkish stare is tempered by a face on the cusp of a smile. He speaks thoughtfully and deliberately and highly articulately, letting seconds of thought drift by before he's ready to articulate an answer.~~

~~As he lifts the book off his shelf: God this thing is too big. It was so hard to write! The book has 11 chapters and it turns out it's much harder than 11 times harder than writing a paper, it's more like 121 times harder than writing a paper.~~

~~[[quote: Uh oh. My freezer is calling me.]]~~

~~The other major strand of his work, looking ahead is to dissect thee evolution of the DNA-binding domain of the steroid hormone receptors – you need this to complete the picture because there is no use in evolving a new receptor-ligand pair if that pair doesn't also switch to regulating different genes.~~

~~So if Thornton still cares so deeply about these environmental issues, as he clearly does, then how does he justify having quit the activist arena that could help solve them? It takes 22 seconds for any kind of answer to emerge. I think people should e free to follow their passions and become what they want to be. [lame so I left it out]~~

~~Me: I think it's kind of cool that you're using the most sophisticated computational techniques to understand something that is millions of years old~~
~~He agrees.~~

~~[[an asideon the 2003 science paper: these hormones are also biochemical intermediates in the pathway that leads to synthesis of oestrogen, so the duplicated receptors basically took advantage of existing ligands, which Thornton calls ligand exploitation]]~~

~~The work also provided a step by step account for something that previously seemed unevolvable.~~

~~Response to 2003 paper~~
~~OR [[One response which Thornton has pinned up outside the lab, read "this is the lamest experiment ever to attempt to show how complexity could evolve." [chk] To which Thornton says he responded, "we're working on much lamer experiments now".]]~~

~~. [[During evolution, the team worked out, each steroid receptor is only as specific as it has to be to bind its target ligand and exclude all others that existed at the time.]]~~
~~Following this pattern….~~