

Rob Desalle 646 226 9675 Jan 30 2012 4.30pm

I work at AMNH, curator here, I also teach at Columbia, in evolution course – he took that at Columbia, and became interested in stuff I was doing, we hooked up, Joe started to hang out with me at the museum and learn phylogenetics, and Joe's work heavily based on phylogenetics and led to training in trees and interpretation of trees. He was here 3-4 years and worked with Darcy Kelly too, he realised he could take a gene in steroid receptor family and do phylogenetics on them – did a 'very very clever' algorithm called LILD it localised incongruence between trees, so usually you have tree for a member (?) of steroid receptor family and another one and can see how different they are – overall incongruence – important to see different evolutionary histories of two receptors

But Joe started to think of incongruence between each tree and focused on a steroid receptor with ligand domain and DNA binding domain, which controls how gene transcribed – so 2 cassettes in each protein and about 50-60 members in steroid receptor family. Build tree, that's cool, but he separated the DNA binding and ligand domain and made two trees and look at incongruent DNA so binding domain evolutionary history and then ligand domain and allowed to test hypotheses these things acting like cassettes – 'now that's cool enough right there, but he went on to see which nodes are different', to see which steroid receptors diverged and showed that they swapped cassettes, He found that it probably evolved as a result of cassette swapping, really good example of Joe's taking something and looking at methods for the whole organisms and using them on genes. **He gets down to the nitty gritty of genes and proteins and then takes it back to the whole organism.** When Joe came to lab worked on Drosophila systematics so we were collecting them and looking at DNA sequence to understand relationships of species to each other, whole organism relationships.

The beautiful thing about what Joe did was to think you could do this with whole organisms can do this with genes?

Published that in **Systematic Biology**

Why Steroid receptors

Steroid R – he thought really hard about it with Darcy, wanted a system a large gene family but not too large eg homeobox genes too large and some other families too small, the sweet spot was steroid R, for no. gene members.

Wanted to take what he did statistically and put it back into animals system to test hypothesis. Darcy, had Xenopus system, so with me and him he came up with this PhD was more Darcy's student than mine, but he split his time, I consider him one of my students, a lot of work, he published had phylogenetic taste

I say he worked in my lab.

Q: wasn't his choice of steroid R influenced by his work with Greenpeace?

In my conversations he enjoyed the reductionism versus the fluffiness. He wanted to use the analytical techniques, His book: **'it's a nice book but a bit fluffy' [called it Pandor's Box], not much quantitative science. I think he wanted to explore that side of your abilities [ie quantitative]**

When did thesis, I think he wanted a narrow topic, to advance his quantitative science, unsure if the book influenced his choice of R family – my interactions mostly I observed an amazing quantitative mind and an amazing grasp on problems

He's a tinkerer. He knows his tools and knows the parts and can play with them. We're all tinkers but we publish in obscure journals. He's able to tinker and make it into a big idea, a big story.. He was writing the book for a couple of years at

start of his PhD that was mostly at Columbia. They have a rough road to get PHD courses and so on

Was at the lab during the day and writing all night?

He could've been. I was shocked when I saw the book. I was just blown away by his quantitative mind. He could've been writing War and peace and I wouldn't have known it. He's intense but there are blasts of humour there – if you blink you'll miss them

Did he lead a green life in NY?

I didn't see that side of him. I knew he was very eco and environmentally focussed but I didn't see that side of him

He was so intense in learning the phylogenetics he really made a spectacular research program. **He could have been going on Greenpeace voyages at weekends and wouldn't have known it**

I expected him to tear up any place he went to [talking about his meteoric rise from then on] I didn't expect the aggressiveness with which he went after creationism.

Have focused on testing evolutionary hypotheses, seemed very technical, to attack ID – need to be technical and have eloquence and ability to communicate with general public, he didn't try that around me

[HP Thought – seems to have found a new campaign to fight]

He's found ways to really attack that silly idea. He has aggressively gone after those yo yos. I think, this irreducible complexity idea, every system Joe has gone after, he's shown how to reduce it. They've never published science, - he has, It's ironic that when you do start doing experiments, it falls apart – I think at a certain point they'll have to abandon it [the irreducible complexity idea]

No, it might not change ID proponents mind, you are going to be able to change the minds of people who teach this stuff in schools eg if you have a judge, if got published science versus nothing, He gave himself some street cred. He'll probably be one of those people asked to debate ID people. He's very articulate and well spoken

What about in class at Columbia?

He stood out, There's no doubt he was the best student in the class

He'd majored in English but it was Yale education did some basic science? He can write like someone who's been in the business for 30 years

Personally, he's really down to earth, he's got 2 or 3 children, moved to Eugene, he's really really interesting guy

I keep in e-mail contact, I read his papers as soon as they're out

I'm really proud of any student who gets a job and a family, I tell them it's important to have a life outside the lab, he's an extremely well rounded individual

Darcy Kelly 31 Jan 2012 4pm

Joe went to Yale then to Greenpeace as director of research

He realised need a background in science, went to Columbia, we have program for English Majors to get into medicine, he wanted to go into science, so went to Col and took courses in med bio etc.

And then applied grad program and accepted

First rotation in my lab, ended up here with experiment and cosponsored with Rob Decsall but physically in my lab

I have nice comfortable lab here cfr museum. He came to the lab, has an interest in sexual differences by which female and male phenotypes become expressed. How

steroid hormone orchestrate that response to become male or female behaviours and expression of steroid hormone receptors in tissues

So we had cloned Xenopus androgen receptor but difficult to align it – has 2 parts to it. He just did it, he's a [something] clever guy – went to Bioessay

He's thinking of way to use this family to understand novelty

St h receptors, if screw up one thing but the entire thing is dead/ How evolve?

He got idea of ligand exploitation. Oestrogen last hormone in pathway was earliest ligand for R. He could find it in cyclostomes – responded in lamprey (cyclostome) [[I think this showed that an ancestral version of the receptor still responded to the hormone]

I was on the Great Lakes committee use anti androgens, he said, are they in invertebrates? Evidence mounting that find metabolic product earlier. **He thinks clearly and writes well** – he could capture metabolic intermediates

And was guy who works with lizard hormone and – went to paper – **Science, first very big paper**

He was also writing this book

I would've hated to be a fellow grad student, he was writing book and publishing in Science and having two children at the same time

Sex differentiation [I asked was it a coincidence that he worked on hormone receptors] was out of fashion, he recognised possibility of working on it. Even as early as first paper was using structure of st h r – prefigured his later approaches

Joe became very clever at figuring out new ways to find new sequences, find consensus sequence

DNA, like a molecular fossil, but can't every go into the past and get the DNA. Can use algorithms to predict ancestral sequences

Then make it and crystallise it

That was the **next phase, reconstruct these ancestral proteins, 2nd most influential paper, ratchet paper**, why can't you go back? Dna has a history, he showed couldn't go back

Metaphor of ratchet is a powerful one

We met with Don someone, casting for a post doc fellowship, he pointed out one at Earth Institute Fellowships, he had strong interest in environmental effects, he applied for one and got it

Even if I hadn't been supervising him in my lab he would've been welcome to have out here

I published 2 papers with Joe, rest was on his own

He did fellowship, great collaborations, in environmental endocrine disruption – led to policy paper

He could think about how to change policy

Endocrine disruptors, expts and time consuming [I think] to.....test for their disruptive effects, are compounds that act like steroids

He came up with some ideas how to test without expt testing

Educated mamas – feeding through glass bottles [ask Joe about BPA]. Tissue cultures, known plastics for a while can be a problem

End disruptors, Xenopus. We never worked on endocrine disruptors.

Biomonitoring of industrial pollutants – body burden 2002 [I think this was the paper]

Implementing green chemistry. McCally & Howard & earth institutes

Postdoc fellowship with Earth institute

Meanwhile, met with Michale Crow, was VP at Columbia then I wanted to offer him job, I was always trying to Columbia to hire Joe. Crow said go elsewhere first.

Offered to fund technician for Joe, so hired someone she went with im to Oregon

He was very productive during those years

At end postdoc, got 3 interviews Oregon, Indian and Urbana, Champagne

3 job offers, **they all moaned when lost him One called me up and sobbed**

Eugene does very good evol biology, lovely place, old hippy town

All very eco friendly. **I remember when he was designing his house and fretting about the greenness of the electrical outlets**

Wife is a successful greek lawyer – been in front of the supreme court, problem was she would be the trailing wife

He hit the ground running, got a junior Hughes, contribute to do ext gd work

He always worked along, his first project on steroid h r. He grabbed an idea, most p think of evolution of organisms but he thought of genes and molecules, He has all these interesting projects, he looks at evolution of ...yeast, push them in one way or another

When he was in my lab st h r, we're not a hot bed of evolutionary biology here, only lab int in evoln was my lab, I work on evol of bhjeaviour, he carved out his own path, I have space to him like a visiting scientist even though he was a first year grad student. I only have 2 papers with him

He didn't write book in the lab, I twas a big deal thing when it came out

He was savagely attacked – blogs websites, from chemical industry. **He'd been in the trenches all those years at Greenpeace, have to be a fighter**

What about intelligent design now?

I asked him to give a lecture, Eric Olsen lecture [sp?], who's an activist – he gave an interesting talk, part science. Where does argument come from for ID? It was abs marvellous [talk]

It's a repugnant idea – it's deeply anti-intellectual [if you're an evolutionary biologist] said he wrote that bit on the place. That s 2006 (?)

Gotten multi[ple awards, he's one of my star children

He was a bit unlikely, with English major

He's beyond intense. He's a very driven guy

He's driven and ambitious but ambitious not the driving force of his personality

He has enough ideas of his own that he can listen to what you say and have a discussion without it being self referential [unlike many in the field, she says]

He had an apartment in Brooklyn, **green parents, they were strolling up and down the green avenues of Prospect Park**

He was home with his wife and family

The most interesting thing was kicking out the book, **it was rather good**

Chicago – trying it out. We tried desperately to get him but Chicago has good schools" Not like NY!

I talk to him about 2x a year about career things

He's certainly more interesting than Francis Collins, I'll tell you that

Talk to his students too that would be interesting

Eugene has Saturday market, children ...I've always told my undergrads

...[something about having a life and children]

He had mixed feelings about this profile, he told me

He has a baby Hughes, supposed to stay where they are, so would lose it if go to Chicago

Could sacrifice, it, you should speak to someone at Hughes about hi, as Tijuana, I'd go straight to the top, ask: Why him? Or ask Sean Carroll – what was it about the work?

Antony Dean interview 31-1-12 5pm

Start with me at the beginning of the field

Review, first of this field I think. Structural basis of molecular adaptation. Biran Galding and me, Review & Diatribe, 15, p 355 Mol Biol Evolution in 1998

Potted history, Dick Lewontin – population genetics, and Pauling, molecular evolution, laid the foundations

These approaches used information in sequences to infer something about evolution of seqs

It's all inference, Don't test it – signature of selection

It bothered a fairly small no of pop ecological geneticists, they wanted to understand it. They were trying to look at the physiological – leading to genetic basis, very difficult, all observed.

First idea, go out and measure selection. Barry Hall and Pat Clarke and others, microbiological looked at microbe adaptation, now strictly experimental approach – adapting things in the lab

Now, fusion of these 3 approaches. It all eventually merged

Seqs to ID sites subject to selection

Exptal – in lab, to manipulate genes

Organisms – see what they do to organisms, and genes

Trying to tie it into ecology

First kid on the block, 3 of us

Shocho Yono [see his e-mail]

Me

Steven Benner

Sho – worked on opsins, how changed when shifted envt – see amino acid replacements occurring in different lineages

Showed changes can change properties of proteins – publication Yokoyama 1990.

He's engineering modern opsins

Ben wanted to build on ancient proteins, he built ancient RNA Jermann 98, found difference, first time someone reconstructed an ancient molecule, turned heads

I look at change of NAD to NADP co-enzyme in E coli, intro 6-7 aa ie engineer it so used NAD instead, - basically as it was 3.5 million years ago.

By mid 90s we've got an incipient field – string papers in PNAS (he published)

And other people were doing things too, eg high altitude Hb in yeast

By 1998, gotten to point where could write a review

It **was the conceptual leap** – not technical advances that facilitated this

Instead of passively observing things as most of evolutionary biologists do you actively go in and test the hypotheses experimentally

Now **Joes in 90s, doing steroid hormones, same stuff, doing a beautiful job**

Then I read his work, I'm suitably impressed

We were reintroducing engineering NAD into NADP E coli [or something] and found selective course of the change Science 2005, Zhu

Steven went onto EFT – type of TFs

H tried making ancient one, see if thermostable ie was ancestor a thermophile and Shoso, then look at IR and UV and started making ancient proteins

You can build two ancestors onw with modern function and ancestral, and mutation which cause functional change 0- might get new amino acid that locks in change

He's done work to lock in changes, irreversibility

Then NRG tanita asked me to write a review and **I thought I've very busy and he can help, gold hold of Joe, you've got a different take**

We had a blast doing it, it was a meeting of the minds

He said we've got to call this something – then people will discuss it, got to have a name

Kicked it around some awful idea and came up with this name – functional synthesis – we gave it a name. coined term

Fuses classic comparative approaches with modern experimental science – key thing one of big problem most evol boil come from genetics or animals and plants. If want study mol evolution have to study phenotype at molecular level, have to become a chemist

Evol biologists run away from chemistry

He's carved out a niche – **he's one of the leading labs, no doubt**

Shozo and me and Jo - big labs

I'm drawn to chemistry and physics, Joe into complexity issues and hanging a go at nailing Behe ie ID

Cf we're looking at evolution of catalysis mech and Shozo, understand opsins evolved and quantum mechanical simulations

Joe – going after complexity

Irreversibility – I think the some things are and some things aren't – I put in 7 aa and made it behave like it did 3.5 billion years ago

Modern NADP engineering to use NAP, then took different enzymes to use NADP, we went in both directions. If you can apply the selection should be able to go back and forth. Diff proteins behave in diff ways, and it's be interesting to see what the rules are

So few cases so far, how find the rule – can't and he wouldn't sit down and say nothing is reversible. **Idea that evolution isn't reversible has been around, to demonstrate it – that's nice and elegant**

A lot of people waking up to this fact ways of doing things Gunter Wagner at Yale, you chat a lot and see each other at meetings – I saw him at Chicago

Is he intense?

Oh yes, he's very intense about his work. He's not the only one

We think making evolution into a real science where you can test hypotheses, really rigorously, that's it's the way physicists and chemists think, something to prove.

There's a passion for the subject, have to have strong background in evol biology and molec boil and protein chemistry – truly interdisc research

I've had reviews say it's just biochemistry, not evolutionary

It's hard work, got to be passionate

Are there critics who say you can never really know how evolution proceeded?

You don't know if you're reconstructed the true ancestry, it's an estimate {?} ..raise their hands and say you don't know it's the correct answer

Phenotype matters even if a few amino acids are wrong
But if go back to certain point, can't align sequences, can't do it, have to use protein sequences

There will come a point where question of unreliability of estimate sequences is sufficiently unreliable, so will say this is an issue, I avoid that, by not doing ancestral [something] and **ideally want to put the protein back into ancestors in ancestral environment – but that's not possible**. We put into modern E coli to Shozo and Joe can't engineer modern

I haven't hear that, we are getting answers that others can't get

Yes there are limitations, but Joe is leading at the moment we're still pushing the field forward

Were now for the field? Challenges?

For me, where did all those proteins come from or RNAs? Joe binds steroids, I bind co-enzymes all binding, How evolution create new catalytic mechanisms? Dream is that it's possible to figure out how flagellum evolved **[ask Joe this]**

Behe says so complex it must have been designed, **evol biologists I say haven't answered Behe's challenge**. All they've said is this protein comes from here. **Putting something together like a flagellum is a pipe dream. I can dream can't I? We've come so far in 30 years**

What about Joe and ID?

I think ID people are – id ont' take them seriously but when he points to flagellum and say evol biologists don't combine to say how it did evolve – **I think Joe is stepping up to the plate and doing about as well as anyone can**

I don't understand why evolutionary biologists respond they way they do, imaging it – not showing how it happened/ he's got a good scientific question and happens to have a ...

He may have more of a social agenda than your typical academic scientist like me. I'm not trying to convince p to change their views on evolution. Joe may have an agenda

Steve Benner is a truly crazy nutcase – speak to him

Shozo too brilliant and modest and diplomatic

I don't; feel every been in competition [I asked him if it was competitive] all in the same boat together

He has adapted our methods yes, he has and all power to him I don't like that cult of celebrity ie as a start – that was my concern in talking to you.