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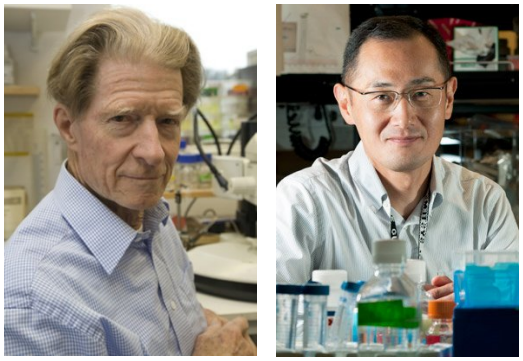
# T-Club

## The Human Embryology & Developmental Biology Newsletter

### Nobel Prize for Physiology or Medicine 2012 goes to Developmental Biologists.

Following the 2007 award of the Nobel Prize for Physiology or Medicine to developmental biologists Martin Evans and Mario Cappechi for the discovery of ES cells and the technology to genetically modify mice, the 2012 award went jointly to Professor John Gurdon of the University of Cambridge and Prof Shinya Yamanaka of Kyoto University. At *T-Club* HQ we are not sure if these two scientists even know each other, and the seminal experiments that defined their research careers were published 42 years apart, but they share a common goal – understanding the basis by which mature cells can be reprogrammed to become pluripotent stem cells.



Profs. Gurdon (left) and Yamanaka (right). Sharing the Nobel Prize, but not the fantastic hair.

John Gurdon's classic experiment (1962) replaced the nucleus of a frog's egg cell with the nucleus of a mature intestinal cell from an adult frog. By showing that the egg then developed into a fully functional clone of its 'parent' (and could go on to produce more cloned 'children'), Prof Gurdon showed that specialised cells are not irreversibly committed to their fate, and that the mature cell still has all the genes and capability required to build a new organism.

Shinya Yamanaka's much more recent discovery showed that by directly genetically manipulating specialised adult cells by forcing them to express as few as 4 'pluripotency' genes, they could be turned back into stem cells and indeed go on to form new cloned mice. These induced pluripotent stem cells (iPS), have the potential to become major resources for gene and stem cell therapy, because it should be possible to derive iPS cells from people with acute or degenerative diseases and use them to regenerate tissues.

Read the official announcement at http://tinyurl.com/cj3wq5s with a summary of the key experiments here http://tinyurl.com/94pacaf

John Gurdon was considered too stupid at school to entertain a career in science – read his school report here http://tinyurl.com/9pglt98

*EDITORIAL…*

*T-Club is the newsletter of the BSc Degrees in Human Embryology and Developmental Biology and BMS (Developmental Biology). We try to feature interesting items of news as they occur, summarise important papers and generally highlight the role of developmental biology and embryological research for understanding human health and disease. Lots of what's in here is relevant to other degrees too.*

*Because this is the first issue for a while, we have included a summary of the Developmental Biology degrees – this is probably especially useful for people at Levels 1 and 2 who want more information about where their degrees are going, and others who want to know what developmental biology actually is.*

*We are lining up a series of 'Where are they now?' articles that will feature graduates from the Developmental Biology degrees, showing you what they are getting up to these days.*

*In future issues we will introduce you to the labs of the teaching team, to highlight the Dev Biol research that takes place at Aberdeen.*

*Martin Collinson – m.collinson@abdn.ac.uk*

# What is Developmental Biology? Who does the degree?

## Developmental Biology degrees at University of Aberdeen.

As with many of the degrees in the School of Medical Sciences, the Developmental Biology BSc comes in two different flavours... either as Biomedical Science (Developmental Biology) or as single-subject Human Embryology and Developmental Biology. The degrees were brought in 4 years ago because research into human birth defects, stem cells, regeneration and wound repair is at the forefront of modern medical sciences, and there was a gap in SMS teaching for students who wanted to work in these fields. There is also a world-wide shortage of the clinical embryologists who work in fertility/IVF labs, for which an embryology and developmental biology training is essential.

What is developmental biology and why is it important? A big element of the subject can be summarised as the study of how the body is built from a single fertilised egg. Problems with the foetus during pregnancy are devastating to families and extremely costly to society.

50% of all early miscarriages are due to genetic defects and 2-3% of babies have birth defects or genetic diseases that will significantly affect the quality of their lives. We need to know how this happens and what can be done about it. In the Developmental Biology degrees, you learn how cells talk to each other, move around and turn into the right tissues at the right time, and also how these processes can be affected by mutations or environmental chemicals.

*T-cut:* If a pregnant mum smokes, there is a significantly higher chance that her sons will be subfertile in later life. Research at Aberdeen has shown that this is because chemicals in tobacco smoke lower the levels of a signalling protein called Desert hedgehog that is required for the stem cells that will produce sperm in later life.

Embryology. But of course, the big questions are not how things go wrong: the more interesting issue is, how do things ever go right? How does a single fertilised egg ever produce a functional, normal baby. In the Developmental Biology degrees you will learn how the embryo sorts itself out - how it 'knows' to make a head end and a tail end, what genes control front and back, why your left is different from your right, and how useful, complicated things like arms and legs, your CNS and all your internal organs form. This really is the business end of human anatomy. Alongside the anatomy and embryology, with the associated physiology that is essential for knowing how the body works, the Developmental Biology degrees train you up in all the core molecular biology techniques that are used in labs around the world to study the key problems relevant to human health and disease.

Stem Cells. Although the Developmental Biology teaching team love embryos more than is perhaps healthy, there is much more to study of the subject than 'just' the embryo. We all come from stem cells, and retain stem cells in our adult bodies where they can be used for repair and regeneration. A major component of the Developmental Biology degrees in your final year is six weeks of lectures on Stem Cells and Regeneration as part of your core course. In the stem cells and regeneration lectures you put the science meat on the bones of what you have read about stem cells in the newspapers and on tv. Where do stem cells come from, what can they do? You are introduced to the embryonic stem cell, and the technology for generation of stem cells from 'normal' tissues. We take you round the sources of stem cells in adult tissues, to the forefront of regenerative stem cell therapy in humans, including gene therapy and prenatal genetic diagnosis of disease.

Cancer. Most human cancers probably have their origins in a stem cell gone bad. All cancers are developmental biology diseases and many scientists who ultimately want to be cancer biologists train initially in embryology and developmental biology. As early as Level 2 (Molecular Biology of the Gene) you will start to learn about the genetic basis of cancer .

Reproductive Biology. With the worldwide shortage in clinical embryologists, there is a real need for graduates with qualifications in embryology and a good knowledge of human reproduction. We're sure you've got it covered, but at Level 3 you have a six week course (DB3501) in reproductive biology, including IVF technology, followed by another 6 week course (DB3803) in early embryogenesis. Many of the embryology and developmental biology graduates go on to pursue careers in fertility labs at here and abroad.

Development and Evolution. As our guest writer in this issue, the ghost of Lonesome George (back page), will confirm, evolution is driven by developmental biology... changes in animal morphology over time in response to the environment are changes in the molecular processes of embryogenesis and postnatal life that control tissue differentiation and patterning. We encourage you to take the Genes and Evolution course at level 2, then at level 4 you take the Evolution and Development course that explores the frontiers of what we know about how evolution and developmental biology are intertwined and how combining the two approaches allows an understanding of the mechanisms by which organisms evolve, which cannot be achieved by either discipline alone.

## Developmental Biology Degrees, *cont*.

### How do the Developmental Biology degrees go?

Most of the dedicated Human Embryology and Developmental Biology teaching takes place at Levels 3 and 4. At Levels 1 and 2 you follow the core compulsory Medical Science courses. Those doing BMS (Developmental Biology) will do Human Anatomy A and B at Level 2. Students doing Human Embryology and Developmental Biology skip the Anatomy courses can do other courses relevant to the degree – take on some Physiology or Animal Biology or Sports Science. Whichever path you take what you should do in your option courses is to learn as much animal and cell biology as you can get it. Levels 1 and 2 should be fun and allow you to explore your interests, so read as widely as you can and get into the biology of animal life as broadly as possible. Animal Planet documentaries are good too – whatever makes you think about animal biology and gets you enthusiastic about learning more. You can also use the Research Skills Course in the second half of Level 2 to do a project on developmental or reproductive diseases that are most relevant to your interests.

At Level 3 the Developmental Biology and Embryology teaching starts in earnest. Even if you didn't sign up for Developmental Biology when you started your studies, you still have the option up to the start of level 3 to swap to Development Biology. Anyone doing any of the BSc Biomedical Science options can swap to BSc (Developmental Biology), and students doing any of the other BSc programmes in the School of Medical Sciences can swap to BSc Human Embryology and Developmental Biology – tell your Advisor of Studies and they will sign you over.

Level 3 kicks off with DB3005 Principles of Development, an introduction to the hows and whys of developmental biology, for example the variety of non-human model organisms that we use to learn about human health and disease, and covering some of the technical and social issues of human embryology. After that there is AN3301 Human Embryology (with the anatomy students) introducing the embryological development of the human body. Alongside this we recommend you take SM3001 Frontiers of Molecular Medical Sciences, which develops your core molecular training as a professional biologist. Second half session takes you into DB3502 Reproductive Biology, followed by DB3503 Patterning the Embryo – your core training in the technology and biology of the human reproductive cycle and the early embryo.

Alongside these you do DB3501 Developmental Genetics and DB3502 Development of Organ Systems, which is a continuation of the programme of work started in AN3301 to understand the molecular and genetic processes controlling how the body is built.

Industrial Placement is a possibility between Levels 3 and 4, for those aiming for an MSci. Once you enter Level 4 you do the Core Course (Advanced Molecules Membranes and Cells) with the final 6 weeks of Stem Cells and Regeneration as described above. Alongside these courses are DB4002 Evolution and Development and PY4302 Developmental Neuroscience, covering the process by which the brain is built, and its relevance to degenerative disease. The second half session is taken up by your Honours Research Project – the jewel in the crown of the BSc degree and where you can finally put all your knowledge into practice as a professional level scientist. Students in the Embryology/Developmental Biology degrees get the same choices of project, in the same pot, as all others doing Biomedical Science subjects, so you don't have to do a developmental project, but we will try to arrange that every student who wants a developmental biology project can get one.

And that's it... write your thesis, sit your exams, and you're done! More than perhaps some other options, the Developmental Biology degrees offer a comprehensive research-based training in modern molecular science techniques for the 21st century. The teaching is done by a dedicated, enthusiastic team who are always willing to answer questions and help you solve problems. To date, around 40% of our graduates have achieved first class degrees and have been snapped up for PhDs and jobs in academia and elsewhere. There appear to be very few unemployed developmental biologists out there.

Any questions about Human Embryology and Developmental Biology or BMS (Developmental Biology) degrees? Contact the Degree Programme Coordinator, Martin Collinson (m.collinson@abdn.ac.uk)

### Where are they now?

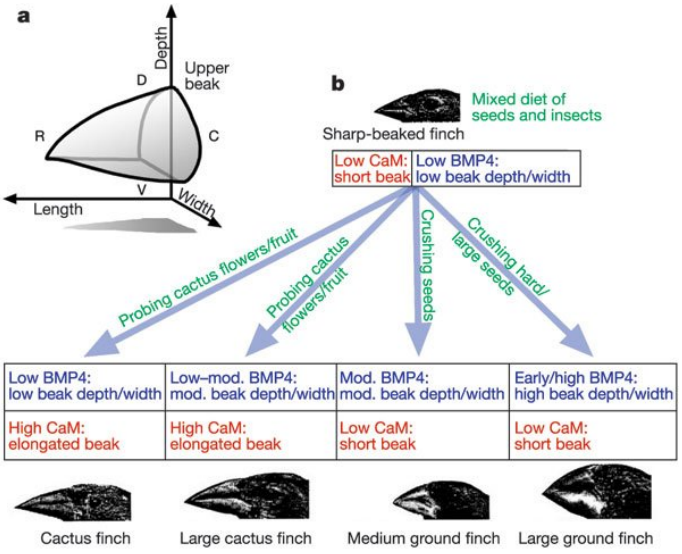
"Upon completion of my degree in Human Embryology and Developmental Biology I secured a job as a Research Assistant working for the Medical Research Council. My job involves creating mouse embryos through IVF, allowing them to develop to the correct stage and then transferring them into pseudopregnant females. It's amazing to see the embryos develop from the one cell stage through to the morula and blastocyst stages. Seeing the results of your work - live pups- is very exciting! High standards of animal care and welfare are extremely important in my job. I enjoy the social aspect of the job and working with lots of different people. In future, my goal is to become an embryologist." - **Phil Page**

# Primitive Streak

Guest writer for our comment and analysis section this time is The Ghost of Lonesome George, the Pinto tortoise.

"I remember the fun the Charles Darwin had, island-hopping around the Galapagos archipelago, eating tortoises (including my Grandad probably) and bopping the local finches on the head with his hat. Of course we didn't have your 'Twitter' in those days, so he had to write a book about it all. Us tasty tortoises rather grabbed his attention at the time, and I really wish he had spent more time with the finches, as in retrospect they proved to be a quite important demonstration of his theory of evolution by natural selection. The different species of Galapagos Finch all look pretty much the same, except they have different bill shapes and sizes – for example the Small, Medium and Large-billed Ground Finches coexist, but with different bill sizes they can specialise in eating different sized seeds in times of drought. What happened is that 100,000 years or so ago, a small population of a boring South American finch arrived accidentally on the Galapagos, and since that time has given rise to all the modern finch species – natural selection acting on them to change their morphology to exploit all the different resources within their environment. There is even one species that has evolved a tiny thin bill and looks like warblers back on the mainland. By it's still a finch, by jingo.

Since Darwin's time, biologists have learned a lot about what molecules and genes control the development of the face, which in birds includes the bill. The signalling protein bone morphogenetic protein 4 (BMP4) is critical for driving cell proliferation in the developing face. Scientists from Harvard Medical School were able to show that the big billed Galapagos Finches had more BMP4 in their upper beaks during development (Abzhanov et al., 2004. *Science* 305: 1462-1465). Their next paper showed that levels of calmodulin (CaM), a protein involved with calcium signalling during development) appear to control the length of the bill – more CaM, longer bill (Abzhanov et al., 2006. *Nature* 442: 563-567).
What's important about this work on an iconic set of species is that it shows that mutations causing small changes in the regulation of genes during development (in this case quantitative up- or downregulation of Bmp4 and calmodulin) can cause significant changes in an animal's body plan (e.g. beak) and hence can be the raw material on which natural selection works to drive evolution. I wish I wasn't too extinct to enjoy it."




a, Developing avian beak is a three-dimensional structure that can change along any of the growth axes. b, A beak of the sharp-beaked finch reflects a basal morphology for *Geozpiza*. The model for BMP4 and CaM involvement explains development of both elongated and deep/wide beaks of the more derived species. Abbreviations: C, caudal; D, dorsal; R, rostral; V, ventral. Taken from Abzhanov et al., (2006. *Nature* 442: 563-567).

# *T*-Club: Putting the 'yo' in the Embryo