Int. J. Dev. Biol. 53: 775-782 (2009)
doi: 10.1387/ijdb.072552cc

THE INTERNATIONAL JOURNAL OF DEVELOPMENTAL BIOLOGY
www.intjdevbiol.com

Skin, cornea and stem cells -

an interview with Danielle Dhouailly

CHENG-MING CHUONG*

Department of Pathology, Keck School of Medicine, University of Southern California, Los Angeles, California , USA

ABSTRACT Danielle Dhouailly received her Bachelor of Science degree (Biology) from Paris University. She then worked on a Ph.D. with Philippe Sengel at Grenoble University. After that, she went to Canada and the USA to work with Drs. M. Hardy, R. Sawyer and H. Sun before going back to Grenoble and starting her own laboratory. In the 1970s, she began a series of creative epithelial-mesenchymal recombination experiments among chicken feathers, mouse hairs and lizard scales, and later between rabbit cornea / mouse hairs. Through these original experiments, she elegantly demonstrated that the dermis initiates the formation of cutaneous appendages, while their type is specified by the class and regional origin of the epidermis. Subsequently she showed that the induction of an ectodermal organ, even in an adult epithelium, provokes the appearance of the related tissue stem cells. These works pioneered the concepts which are used in stem cell biology today. Her laboratory now works on the molecular mechanisms underlying these processes. Her papers are typically characterized by an initial insightful observation, followed by rigorous experiments and thoughtful discussions. They are rich with different shades of perspectives, almost like a piece of impressionist art. She loves gardening and her pets. She considers herself a good observer and hard worker driven by curiosity. Her best moments occur when she suddenly becomes enlightened as to an explanation of a basic concept when looking at experimental results or discussing ideas with colleagues. She believes that good results last forever, although interpretations can change. Her advice to young scientists is to be rigorous at the bench, to think hard, and not to be shy to speak up. The following is the story of how this young, female naturalist grew into a well-respected developmental biologist.

KEY WORDS: *feather, scale, hair, development, evolution*

Danielle Dhouailly was born in Tunisia. In her childhood, she was a little naturalist. She loved to grow plants and watch little animals. She had raised chicks, insects, lizards etc. (Fig. 1). Later she got her B.Sc. degree in Biology from Paris University, next to the Botanical Garden. She moved to Grenoble University (France) in 1965 to carry out her PhD research with Philippe Sengel, who was just starting his laboratory. There Dr. Dhouailly won her *"Thèse d'Etat"* (an honor in France, when she completed fourteen original papers as a first or single author). After that, she went to Canada to work first with Margaret Hardy on the effect of retinoic acid on epidermal appendage morphogenesis. Then she went to South Carolina (Fig. 2) in the United States to work with Roger Sawyer on *scaleless* chicken mutants. Finally she went to work with Dr. Henry Tung-Tien Sun in New York University to learn a lot about keratins (Fig. 3). Back to France in 1987, she started her own laboratory in Grenoble (Figs. 4,5).

Dr. Dhouailly's work is characterized by bold creativity and insight. In the early seventies, she pioneered the epithelial-mesenchymal recombination explants using epithelia and dermal components from different chicken and duck skin, or made chimeras among chicken, mouse, and lizard skin. Through these original experiments, she elegantly demonstrated that epidermis and the amnion ectoderm can be induced by the dermis to form ectodermal organs, of which specific fate is dictated by the ectodermal class. More surprisingly, her laboratory discovered that the adult rabbit cornea can also respond to the dermal signals which trigger the formation of mouse hairs. The cornea cells lose their cornea characteristics and start to express keratinocyte phenotypes. These experiments pioneered the concepts used in stem cell biology today. They also provide insight that we may be able to use the amnion, cornea, skin or other epithelia for tissue engineering of different ectodermal organs.

***Address correspondence to:** Cheng Ming Chuong. Department of Pathology, Keck School of Medicine, University of Southern California, Los Angeles, California 90033, USA. Fax: +1-323-442-3049. e-mail: cmchuong@usc.edu - web: http://www-hsc.usc.edu/~cmchuong

Published online: 8 June 2009.

ISSN: Online 1696-3547, Print 0214-6282

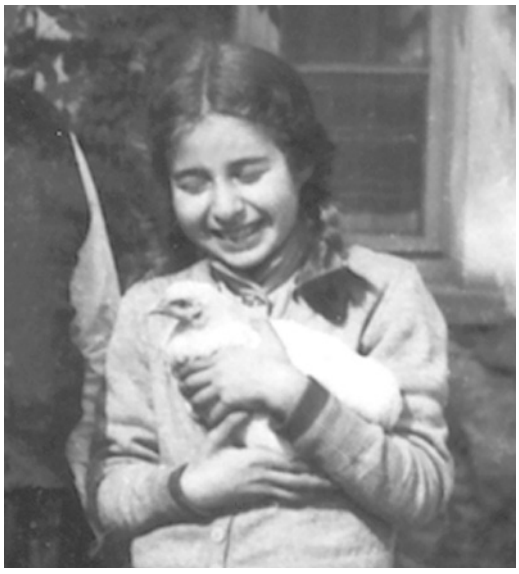


Fig. 1. Danielle Dhouailly (1956), *in Tunisia holding a chick pet named "Pascaline".*

Fig. 2. Danielle Dhouailly (1983) *during her stay with Roger Sawyer in South Carolina, USA. Photographed with a cat named "Gremlin".*

Her papers typically start with an interesting biological phenomenon, followed by some elegant and rigorous experiments, and finish with thoughtful discussions. The discussion is usually rich with different shades of thinking, almost like a piece of impressionist art. She is a rare individual whose work bridges classical experimental embryology with modern molecular biology era. She contributed significant work to the book "Morphogenesis of Skin" (Sengel, 1976) and in 2004, she edited a Special Issue of *The International Journal of Developmental Biology* entitled Skin Development (see Dhouailly *et al.,* 2004 and related papers), which includes a review of classical phenomena and updates progress in molecular biology.

Professor Dhouailly considers herself a good observer and hard worker, driven by curiosity in nature. She believes that good results are facts that will last forever. The interpretations though, will change because they are based on the evolving scientific knowledge. When she was young, she struggled with the difficulty of being a female professor in a male-dominated profession. Later she had to battle against cancer. Despite these difficulties, she managed to get science done. She loves science, particularly at times when she had a sudden "enlightenment", meaning that an explanation for a fundamental problem suddenly appeared when she was examining experimental results or having a discussion with students or colleagues. This is what she calls the "honey" moment. Here is the story of how this young naturalist has grown into a respectable developmental biologist, and one of the few early female "Exceptional Professors" in France.

You started your research career with Philippe Sengel. Your work together culminated in the influential book "Morphogenesis of Skin" in 1976 which summarizes the classical experimental embryology works on skin morphogenesis up to that day. The book set the foundation for the field of skin pattern formation. Would you introduce some of the people of that day and the atmosphere of the laboratory?

Professor Philippe Sengel had broad interests in developmental biology and carried out many projects in his laboratory which were very different. There were several persons within the research staff in his laboratory, but only three were working on skin directly: Annick Mauger (the formation of dermis), Annick Thevenet (wound healing) and myself (feather morphogenesis). Raymond Saxod was working on a related model (skin innervation). Madeleine Kieny and her student, Marie-Paule Pautou, did excellent work on the morphogenesis of the chicken limb bud and enjoyed international recognition. Désiré Bullière was working on cockroach regeneration. He was a very good scientist with original, new ideas about cell positions. Unfortunately he later left research for family reasons. The projects of other people include morphogenesis of trout, imaginal disks in *Drosophila*, formation of ovary in Ciona, teeth in amphibians, and cell cycle control in amphibians.

Dr. Sengel was excellent in foreign languages, and his laboratory was one of the first in France to publish papers in English. Another good thing in his laboratory was the organization of the technical staff. There was a technician for each of the following fields: histology, sterilization, photography, library and editing / publication, plus a washing woman and a handyman. For the book “Morphogenesis of Skin” (1976), I myself and the librarian, Michelle Brugal, worked together an entire year to help finish it. So you can see there was a good mixture of interesting biological projects and people. However, later I was also the only one who continued to pursue the tradition of Developmental Biology.

Early in your career, you started a series of very interesting experiments by doing epithelial-mesenchymal recombination between mice, chickens and lizards. Would you please tell us what you learned from that work and the implications of that work today?

Part of my PhD thesis was to recombine embryonic dermis and epidermis between chick and duck. I did this because I wondered whether epidermis or dermis is in charge of the architecture of epidermal appendages. I obtained feathers whose architecture was completely defined by the nature (origin) of the dermis. I remember that Philippe Sengel thought my results were unbelievable initially. I was shy but I was confident about my experiments and took pride in my findings. Eventually I had to tell him: *“So, I might be the cleverest forger in the world, but could you please increase the magnification of the microscope and examine the evidence for yourself? This chimeric feather with spiny barbules is entirely constituted by duck epidermal cells; but it has no rachis, implying that the architecture is of the chicken type of feather.”*

Since then, I became more independent in doing my research. To understand what the dermis is doing during feather morphogenesis I thought I would have to increase the difference between the origins of the two skin components in epidermal / dermal recombinants. So I started to do recombination experiments with epidermis and dermis from different classes of embryos including mouse, lizard and chicken. One sunny summer day, I was examining the results of these recombinants. I got hair buds, scale buds, feather buds, according to the origin of the epidermis, whereas the control recombinants showed hair follicles, perfect scales and complete feathers. What a clear result! Suddenly I understood. There were at least two different steps in the formation of skin appendages: make an appendage first, and then construct the phenotype of this appendage (Dhouailly, 1975). This day remains one of the best days in my life. I think it is this kind of thrill and understanding of nature that keeps me going as a scientist.

When I told Dr. Sengel about this work and its conclusion, he just whistled. Later he used this idea in the book "Morphogenesis of Skin" (Sengel, 1976). Even today, in the introduction section of most papers on skin development, the idea that there is a continuous dialogue between the dermis and the epidermis is usually referred to by citing Sengel (1976) or Hardy (1992). To my disappointment, my own review (Dhouailly, 1977), where I moreover suggested an active role also for the epidermis, went unnoticed by the scientific community.

The wonderful implication of this work today was revealed by you Ming [Cheng Ming Chuong], your work principally, and also that of others, like Bruce Morgan, Paul Goetinck, Irma Thesleff etc., who have found some of these molecular signals which are exchanged between epidermis and dermis. It is satisfying to see this progress even though the whole story is not completed yet (reviewed in Lin *et al.*, 2006). In the adult feather follicle, your laboratory even found how a rachis forms, with a balance between BMP4 and Noggin, and the slope of a Wnt 3a gradient (Yu *et al.*, 2002; Yue *et al.*, 2005). Since the presence of a rachis is the main difference between the chick and duck embryonic feather, I bet you that there will be differential expression in the dermal condensation between these two species.

Fig. 3. Danielle Dhouailly (1986). *Photographed with Dr. Henry Tung-Tieng Sun in Orlando, USA.*

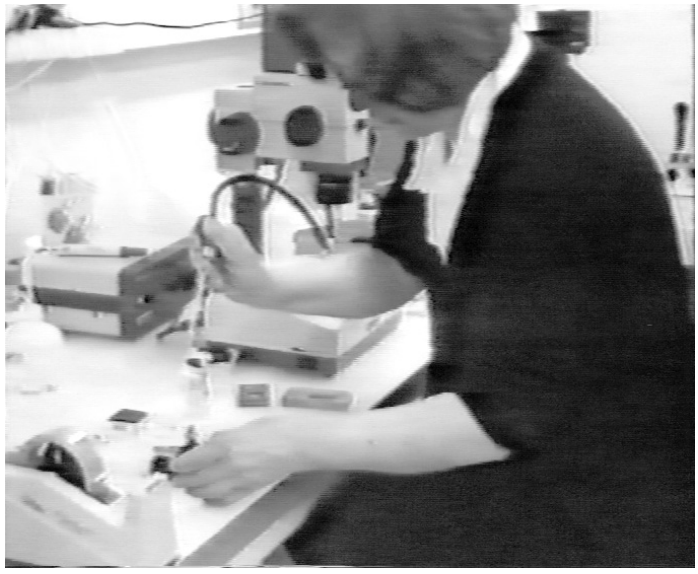


Fig. 4. Danielle Dhouailly (1990), *working with chicken embryos at a bench in Grenoble University (France).*

These days there are of course many laboratories that work on mouse hairs (reviewed in Millar, 2002; Schmidt-Ullrich and Paus, 2005). As I predicted in the seventies, some signals are similar between birds and mammals during the process of primordia morphogenesis. However, some signals are different in the very early stage. I am working on this problem with Sebastien Cadau, one of my two latest PhD students.

Later you did the scale / feather transformation work and the cornea / hair trans-differentiation work. These studies actually pioneered the concept of stem cell biology in use today. Would you tell us more about these works and their significance today?

I will answer this in two steps, although both transformation events concern, you are right, the plasticity of epidermal fate.

In the late seventies, I was working with Margaret Hardy about the effect of retinoic acid on mouse skin. On the side, I was curious to know what could be the effect of retinoic acid on chicken skin. Thus I started to inject retinoic acid into chicken embryos at two embryonic stages, which correspond to the beginning of feather (embryonic day 7) and scale (embryonic day 10) morphogenesis. Upon cracking the eggs later, only some of the embryos with later injections survived. However, the three to four scales which started to form at embryonic day 10 now became feathery scales! Later I pursued this work further with my PhD student, Benoit Kanzler. It was found that several types of perturbation led to formation of feathers on chick foot scales (reviewed in Prin and Dhouailly, 2004). How the signaling pathways are altered to form feathers or scales is still unclear, but it seems easier to form complex feathers than simple scales on an avian epidermis. These results helped shape my point of view: avian ectoderm is more programmed toward forming feathers, and mammalian ectoderm is programmed more toward forming hairs. The other ectodermal derivatives, like cornea, scales, glands, etc. appear to have an inhibitory mechanism of this basic program (Dhouailly, 2009).

The implication of this work today is enriched by the Evo-Devo

perspective of feather origin which you have highlighted. Recently a new exciting fossil was found in China: a feathered dinosaur with flight feathers in both forelimb and hindlimb (Xu *et al.*, 2003)! I was delighted to hear that. In the last meeting of Vertebrate Morphology at Paris in July 07, I met Dr. Alibardi, who is an expert of skin evolution. I thought it would be a good opportunity to convince him that avian scales are not directly related to reptilian scales, but are a result of convergent evolution. No way! Although I presented all my arguments in my talk, especially the evidence I prefer the most: the formation of a feathered skin by amniotic membrane cells only, a data obtained in my laboratory by Ingrid Fliniaux and Jean Viallet (Fliniaux *et al.,* 2004). The graft of Noggin and Shh producing cells in the future amnion results in the inhibition of BMP4 expression in the ectoderm, and allows the proliferation of the mesoderm to continue until they form a dense dermis.

Fig. 5. Staff in Danielle Dhouailly's first laboratory in Grenoble University (1991). *(From left to right): assistant professor, Dr. Jean Jacques Michaille, now a Professor in the University of Burgundy; student Isabel Pavitt, now working for a scientific journal; PhD student Catherine Chaloin-Dufau, now a professor in a high school; Professor Danielle Dhouailly; PhD student Jean P. Viallet, now an Assistant professor in the Dhouailly laboratory.*

Now let us talk about corneal epithelium. I was attracted by the cornea model when I worked with Henry T.T. Sun. At that time, Henry had just discovered that different pairs of keratins were preferentially expressed in different types of epithelia (Tseng *et al.*, 1982). As an embryologist who was taught about the "determination" concept, I wondered when the corneal epithelium was determined to produce its specific keratins, K3 and K12. My PhD student, Corinne Ferraris, together with a previous PhD student, Catherine Chaloin, started to perform recombinants between mouse dorsal embryonic dermis (a hair-inducing dermis) and rabbit corneal epithelium at different stages. I chose these two species so we can be sure about the origin of the differentiated cells (the distributions of their chromatins in nuclei are different and can be recognized). Then one day, Corinne told me: *"I am sorry, Danielle, embryonic rabbit cornea produces hairs (upon recombination), even the adult rabbit corneal epithelium produces hairs"*. This was unexpected. This is a wonderful result. Nature is trying to tell us something.

The problem was to have this work published. The first time I submitted the manuscript was in 1994. The paper was not accepted and I had to try other journals in the following years. Each time we were rejected with the comment: the results are unbelievable. So, I needed to have somebody watching the work to avoid any mistake. Colin Jahoda was visiting my laboratory at the end of the nineties. I asked him to verify the results. Eventually, we published the work in Development (Ferraris *et al.*, 2000).

After that, I asked a new postdoctoral fellow, David Pearton, to work on the mechanism. At the beginning, he was reluctant and asked for other projects. However, after trying some recombinants and seeing the results for himself, he was enthusiastic about it. Subsequently, he showed (Pearton *et al.*, 2005) that when cells from the base of the central corneal epithelium are in contact with dermal cells, they express β-catenin and stop synthesizing corneal keratins. These cells are now able to form placodes and attract more dermal fibroblasts to form a dermal condensation. These novel placode cells cease expressing Pax6 and proliferate to form hair pegs. Finally, the emergence of epidermal cells expressing K10 from the novel hair follicles demonstrates the formation of hair stem cells by the outer root sheath.

The implication is that, for the first time, it was demonstrated than in mammals, differentiating cells are able to go backward to a stem cell state, and that the formation of an "organ" like a hair follicle, involves the segregation of cells that take on and keep a stem cell status. This work also shows the possible switch between different types of stem cells, at least between cells originating from a same embryonic layer: in the present case, the ectoderm. I am persuaded that there are different levels of stem cell status in adult tissues: some constitute a reservoir and are triggered only in case of emergency, some are *en route* to differentiation, but are still endowed with proliferation potency and can be easily turned backward, as in the case of the basal cells of mammalian corneal epithelium. The latter, as recently demonstrated by Yann Barrandon's laboratory, are used for corneal epithelium homeostasis in normal conditions (Majo *et al.,* 2008). There are different other ramifications. Remember my idea about how the mammalian integument is more programmed toward forming hairs? In the case of cornea, a beautiful work by Mukhopadhyay *et al.* (2006) showed that this part of the integument is prevented to form hairs by the local expression of an inhibitor of Wnt signaling, Dkk2. Indeed, the null mutant for Dkk2 had no cornea. Instead, a true hairy skin formed in front of the lens.

One important issue is to show what the differences between corneal and epidermal stem cells are. This involves an understanding of how the ectoderm becomes a corneal epithelium during early embryonic development. This is the subject of one of my recent two PhD students, Elodie Collomb.

A more general ramification could be to work with other types of tissue stem cells. Why not try to induce a switch from intestinal stem cells to the formation of pancreatic islands? In the stem cell biology field, the emphasis has been on the potentialities of embryonic stem cells. They have been shown to be able to give rise to every type of cell, but currently who can obtain 100% differentiation to produce a given cell type? I think it should be

easier to work with adult stem cells, even if their potentialities are more limited than embryonic stem cells. An important direction is to understand the eventual links between embryonic and adult stem cells. There exist several steps in the differentiation process, the first one being the formation of the embryonic layers. One could imagine that stem cells could be segregated at each step: either that the embryonic stem cell state remains in some groups of isolated cells, or better, that during embryogenesis some cells are segregated in the tissue. Even within a differentiating tissue, cells that have not yet become post-mitotic keep open the possibility of going backward.

In the case of corneal epithelium, we showed that signals from an embryonic environment are able to reprogram basal corneal cells to epidermal stem cells. Two groups report today that they have reprogrammed skin cells into ES cell- like stem cells, by inserting four genes (Yu *et al*, 2007; Takahashi *et al.,* 2007). It will be still more wonderful to find which signaling might activate those genes, thus to perform such a reprograming without genetic alterations.

Your work is usually creative and inspiring. Can you share with us your thinking process of formulating a project or a paper? How are they conceived? How do you ask questions?

Ming, I do not deserve such words. I am just curious and lucky, and was a very hard working girl. I always told my students: believe your results and ask questions. Do not be blind by what is taught in the developmental books or reviews. When experiments are done correctly, their results are there forever. In the future, they may be interpreted in another way, depending on the general level of knowledge which increases every year. For the young fellows who enter the field now, they now have new and wonderful tools, which should allow a better analysis of previous results.

During my research career, I approached science in the followed five different ways:

Take an old experiment, for example the formation of supernumerary feathers following the graft of neural tube in the chick midventral apterium (Sengel and Kieny, 1967) or in the amnion (Dhouailly, 1978), and find what are the molecular signals (Fliniaux *et al*., 2004).

Another example: we find that Wnt1 signaling from the dorsal neural tube was required for the determination of dermal cells from the somite dermomyotome (Olivera-Martinez *et al*., 2002). This was the explanation for an old previous result, the formation of a large apterium, following the excision of the neural tube (Mauger, 1972).

Take an old dogma or model which has been neglected for many years, and work on it with new tools. In the case of the induction of the cornea by the lens vesicle (review by Hay, 1980), recently we found that the lens vesicle is not only the cornea inducer, but even delays stroma cell migration (Ying *et al*., in preparation).

When you get an unexpected phenotype, try to understand what happens with a sequential study or by changing the experiment parameters (my early work, and more recently cornea experiments).

Compare with what happens in a different model. One example, at the beginning of the nineties, I thought that FGF shown as an inducer of mesoderm in *Xenopus*, could also play a role in feather formation. Unfortunately the FGF2 protein was quite expensive and I asked my student to dilute it. I was wrong. We got no result at all. By that time, you have the same idea, and got the formation of supernumerary feathers in semi-apteria (Widelitz *et al*., 1996). Using your concentration for FGF2 and scaleless embryos, we then showed that FGF2 is a permissive factor, allowing feather or scale morphogenesis depending on the skin region (Dhouailly *et al*., 1998.)

Even when you are doing ordinary or routine experiments, still keep your eyes wide open. In case of some unexpected result, try to understand it (e.g, when we did our cornea work). This is the *honey* in research.

There is also another very important rule: listen to your PhD students. My youth had taught that to me. Young researchers can have a new perspective on old problems. Even if you are surprised and unsure, do not tell them that they are crazy. Just tell them that they have to test their idea, and that they are taking a difficult, dangerous, but exciting path. This recently happened in my laboratory. We showed that instead of acting as inhibitors, different BMPs play distinct crucial roles, ranging from the regulation of dermal condensation formation to the continuation of feather morphogenesis (Michon *et al.,* 2008).

You recently edited an excellent Special Issue of The Int. J. Dev. Biol. entitled "Skin Development". Can you tell us the background of that Special Issue? It must have given you a chance to reflect upon the progress of the field. Would you

Fig. 6 (Left). Danielle Dhouailly (1995) *had the joy of having her laboratory recognized by the CNRS (Centre National de la Recherche Scientifique). Photo in Grenoble.*

Fig. 7 (Right). Danielle Dhouailly (1999) *at the French Society for Developmental Biology Congress which took place in September in a small town, Dourdan, near Paris. Dhouailly argued with Benoit Robert (back), while Jean-Antoine Lepesant stood by with a smile.*

Fig. 8. Danielle Dhouailly (2005) *attending the Gordon Conference on epithelial cells which took place in Tuscany in June. Dhouailly (left) with Angela Christiano (middle) and Cheng-Ming Chuong (right).*

tell us your feeling about the field? What kind of progress can we expect in 5 years, 10 years, 20 years?

The idea of the special issue on Skin Development happened when I met Prof. Juan Arechaga in a congress. It was after the meeting about skin signaling that I organized in The French Alps in 2000. I thought it was time to bring together all the fantastic progress done in this area during the 1990s, especially by your laboratory. I was fighting cancer at the same time. Hence, I would like to thank Professor Arechaga, who had to push me at the time.

About the progress in the field, it happens every week. Developmental biology studies were sleeping in the 1980s, and then suddenly the field exploded. It is very fascinating. In four years I will be retired, but I will keep in touch. I think by ten years skin and cornea engineering will be done. About basic science in the field, in about 5 years, apart from the understanding of pathway interactions, I cannot predict. You are younger than me, so I return the question to you: what are your feelings about the next decade?

C.M.C: I agree with you that we will have a good understanding of the molecular pathways involved in building feathers or scales, as well as hairs or glands. With progress in genomics and epigenetics, I anticipate we will gain new understanding of the molecular basis of regional differences which will allow scientists to obtain different epidermal appendages in the same species. With that type of understanding, scientists will be able to engineer epidermal cells into different ectodermal organs as you suggested.

Today, there are sophisticated technologies in genetically engineered mice or bioinformatics. If a young scientist is fascinated by biological patterns and contemplating to enter this field, what advice would you give?

Frederic Michon, one of my PhD students, who defended his thesis in September 2007, is in this category. He is fascinated by biological patterning. When in my laboratory, he started to collaborate with a mathematician, Loic Forest, to work on pattern formation. Professor Irma Thesleff just got some exciting results with genetically engineered mice (personal communication) and Michon joined her in Helsinki. Thus my advice to young fellows is also embedded in your question: work on genetically engineered mice and collaborate with bioinformaticians.

Can you tell us your experience as a woman scientist trying to establish her career? Would you offer some advice to female scientists?

This question has been previously treated on a large scale by a series of Fiona Watt interviews with different female scientists (Dhouailly, 2004). Thus I will just repeat my previous answer. Among Professor Sengel's PhD students, the men had become Professors easier. I was the only one among the women to ever become a Professor. In the 1990's, only 5% of university biology professors in France were woman. It was very difficult for a woman: for nearly twenty years I remained the only female Professor in Biology in Grenoble University. Before President Sarkozy who has decided that universities should have more autonomy, there were two possibilities in France to get a Professor position and be promoted: first is with a National Committee for Universities, and if rejected, the second is with a local competitive exam. Thanks to the support of the National Committee for Universities during my whole career, I now have reached the highest rank of Exceptional Professor.

Things are changing fast, and I believe now it is not more difficult for a woman to set up her own laboratory, even in a country like France, Italy, or Spain. The National Committee for Universities in Paris in the 2003-2007 Cell Biology section, consisted of nine women and eight men at the professorial rank. Thus,

Fig. 9. Danielle Dhouailly (2006), *celebrating her 60th birthday with friends in the French Alps in summer. From left to right: PhD students Sebastien Cadau, Frederic Michon and Elodie Collomb; Danielle heading the table; PhD student Nicholas Chartier; Iconographer Brigitte Peyrusse; assistant professor Muriel Jacquier Sarlin and* Int. J. Dev. Biol. *Editor-in-Chief Juan Aréchaga.*

BOX 1

RESEARCH LANDMARKS

Year	Significance	Reference
1975-1977	Demonstrate that phenotype for skin appendages is mainly dictated by the dermis	Dhouailly, 1975, 1977
1980-1984	Retinoic acid lead feathers to form on the chicken scales	Dhouailly *et al*., 1980; Cadi *et al*., 1983
1998-2004	The molecular basis of dermis formation	Olivera-Martinez *et al*., 2002; Fliniaux *et al*., 2004
1992-2005	Demonstrate adult cornea basal cells can trans-differentiate into hair follicle cells by hair forming dermis	Ferraris *et al*., 2000; Pearton *et al*., 2005
2004	Edit special issue "Skin Development" which summarize the major progress since Sengel's "Morphogenesis of Skin" in 1976	IJDB volume 48, 2004
2009	Synthetizing forty years of research, propose a new scenario for the evolutionary origin of vertebrate ectodermal organs	Dhouailly, 2009

my advice to female scientists is: do not postpone the time to be pregnant, you can do both: your family and your career. Some of my past PhD students, or post-doctoral co-workers are indeed young mothers as well as successful scientists (e.g., Isabel Olivera-Martinez, Sandrine Fraboulet) or successful pharmaceutical staff (Sandrine Rhetore).

Can you share with us the most joyful moment and the frustrating moments in your career?

I have had a lot of joyful moments throughout my career: e.g. when I look at experimental results or discuss with my coworkers, and suddenly the explanation appears; when my laboratory was recognized by CNRS (Fig. 6); when I meet and discuss with friends who share research interests, like you (Figs. 7,8,9). Of course, there are also frustrating moments. The worst moment was when I was treated like a forger for supporting a forger (my PhD student) for our cornea work. Even the best researchers can be blind when the results open up in an unexpected direction.

What do you do as hobbies outside science?

I became a naturalist at an early stage, and I have always loved gardening and watching birds or insects. I raised chicks, lizards, insects, and have had two dogs and six cats up to now. I never bought cats or dogs. They meet and adopted me in summertime when they were thrown away by their owners. I am very interested in studies about capacities of animal brains. I like to propagate plants by cutting, especially old roses found in deserted gardens. I love all aspects of life and I am also attracted by the part of archeology that analyzes how we lived in the past. France is very rich in the past architecture. I take pictures of humble but typical houses or farms, which one after another are disappearing or being badly renovated. Thanks to digital cameras, now I am not limited by the cost of film! In my youth, I was attracted by art and had thought of becoming an artist painter. I have good hands, but recognize that I am not gifted in this regard. I am just good at observing. Embryos and feathers are so beautiful to look at under the microscope that I became a skin developmental biologist.

What is your motto in doing science?

My motto in doing science is that *good results are forever*, it is just their interpretation that can change, depending of the evolving scientific knowledge. Thus my advice for PhD students is to be rigorous at the bench, to think hard by themselves and not to be shy to speak up.

Acknowledgments

I wish to thanks all my friends including those I have not cited in this text: scientists, pharmaceutical executives, technicians, students, and especially the work friends of an entire life, Jacqueline Lana, a secretary, then an accountant, and Brigitte Peyrusse, a photographer, then an iconographer.

References

CADI R, DHOUAILLY D, SENGEL P. (1983) Use of retinoic acid for the analysis of dermal-epidermal interactions in the tarsometatarsal skin of the chick embryo. *Dev Biol.* 100: 489-495.

DHOUAILLY, D. (1975). Formation of cutaneous appendages in dermo-epidermal recombinations between reptiles, birds and mammals. *Wilhelm Roux's Arch. Dev. Biol.,* 177: 323-334.

DHOUAILLY, D. (1977). Dermo-epidermal interactions during morphogenesis of cutaneous appendages in amniotes. *Front. Matrix Biol.* 4: 86-121.

DHOUAILLY, D. (1978). Feather-forming capacities of the avian extra-embryonic somatopleure. *J Embryol Exp Morphol.* 43: 279-278.

DHOUAILLY, D. (2004). Interviewed by Fiona M Watt. Woman in Science: J Cell Sci. 117: 1873-1874.

DHOUAILLY, D. (2009). A new scenario for the evolutionary origin of hair, feather and avian scales. *J. Anat.* 214: 587-606.

DHOUAILLY, D., OLIVERA-MARTINEZ, I., FLINIAUX, I., MISSIER, S., VIALLET, J.P. and THÉLU, J. (2004). Skin field formation: morphogenetic events. *Int. J. Dev. Biol.* 48: 85-91.

DHOUAILLY, D., Hardy MH, Sengel P. (1980) Formation of feathers on chick foot scales: a stage-dependent morphogenetic response to retinoic acid. *J Embryol Exp Morphol.* 58: 63-78.

FERRARIS, C., CHEVALIER, G., FAVIER, B., JAHODA, C.A., DHOUAILLY, D. (2000). Adult corneal epithelium basal cells possess the capacity to activate epidermal, pilosebaceous and sweat gland genetic programs in response to embryonic dermal stimuli.*Development* 127: 5487-5489.

FLINIAUX, I., VIALLET, J.P., DHOUAILLY, D. (2004). Signaling dynamics of feather tract formation from the chick somatopleure. *Development,* 131: 3955-3966.

FLINIAUX, I., VIALLET, J.P., DHOUAILLY, D., JAHODA, C.A. (2004). Transformation of amnion epithelium into skin and hair follicles. *Differentiation* 72: 558-65.

HARDY, M.H. (1992). The secret life of the hair follicle. *Trends Genet.* 8: 55-56.

HAY, E.D. (1980). Development of the vertebrate cornea. *Int. Rev. Cytol.* 63: 263-322.

LIN, C.M., JIANG, T.X., WIDELITZ, R.B., CHUONG, C.M. (2006). Molecular signaling in feather morphogenesis. *Curr Opin Cell Biol.* 18: 730-741.

MAJO, F., ROCHAT, A, NICOLAS, M., ABOU JAOUDE, G., BARRANDON, Y. (2008). Oligopotent stem cells are distributed throughout the mammalian ocular surface. *Nature* 456: 250-254.

MAUGER A. (1972) Rôle du tube neural dans le développement du plumage dorsal de l'embryon de poulet. *Wilhelm Roux's Archiv* 170: 244-266.

MICHON, F., FOREST, L., COLLOMB, E., DEMONGEOT, J., DHOUAILLY, D., (2008). BMP2 and BMP 7 play antagonistic roles in feather induction. *Development* 135: 27097-2805.

MILLAR, S.E. (2002). Molecular mechanisms regulating hair follicle development. *J. Inv. Derm.* 118: 216-225

MUKHOPADHYAY, M., GORIVODSKY, M., SHTROM, S., GRINBERG, A., NIEHRS, C., MORASSO, M.I., WESTPHAL, H. (2006). Dkk2 plays an essential role in the corneal fate of the ocular surface epithelium. *Development* 133: 2149-2154.

OLIVERA-MARTINEZ I, MISSIER S, FRABOULET S, THÉLU J, DHOUAILLY D. (2002) Differential regulation of the chick thoracic dermal progenitors from the medial dermomyotome. *Development* 129: 4763-4772.

PEARTON, D.J., YANG, Y., DHOUAILLY, D. (2005). Transdifferentiation of corneal

epithelium into epidermis occurs by means of a multistep process triggered by dermal developmental signals *Proc. Nat. Acad. Sci. USA* 102: 3714-3719

PRIN F., DHOUAILLY, D. (2004). How and when the regional competence of chick epidermis is established: feathers vs. scutate and reticulate scales, a problem en route to a solution. *Int. J. Dev. Biol.* 48: 137-148.

SENGEL, P. (1976). Morphogenesis of skin. In *Developmental and Cell Biology series* (ed. M. Abercrombie, D. R. Newth and J. G. Torrey), pp. 1-269. C. U. Press.

SENGEL, P., KIENY, M. (1967). Production of a supplementary pteryla in the chick embryo. I. Morphologic study. *Arch Anat Microsc Morphol Exp.* 56: 11-29.

SCHMIDT-ULLRICH, R., PAUS, P. (2005). Molecular principles of hair follicle induction and morphogenesis. *BioEssays* 27: 247-261.

TAKAHASHI, K., TANABE, K., OHNUKI M., NARITA, M. ICHISAKA T., TOMODO K., YAMANAKA S. (2007). Induction of pluripotent stem cells from adult human fibroblasts by defined factors. *Cell* 131: 861-872.

TSENG, S.C.G., JARVINEN, M.G., NELSON, W.G., HUANG, J-W, WOODCOCK, M.J., SUN, T-T. (1982). Correlation of specific keratins with different types of epithelial differentiation: Monoclonal antibody studies. *Cell* 30: 361–372.

VIALLET, J.P., PRIN, F., OLIVERA-MARTINEZ, I., HIRSINGER, E., POURQUIE, O., DHOUAILLY, D. (1998). Chick Delta-1 gene expression and the formation of the feather primordial. *Mech Dev* 72: 159-68.

WIDELITZ, R.B., JIANG, T.X., NOVEEN, A., CHEN, C.W.J., CHUONG, C.M. (1996). FGF induces new feather buds from developing avian skin. *J Invest Dermatol* 107: 797-803.

XU, X., ZHOU, Z., WANG, X., KUANG, X., ZHANG, F., DU, X. (2003). Four-winged dinosaurs from China. *Nature* 421: 335-340.

YU J., VODYANIK M. A., SMUGA-OTTO K., ANTOSIEWICZ-BOURGET J., FRANE J. L., TIAN S., NIE J., JONSDOTTIR G., RUOTTI V., STEWART R., SLUKVIN I. I., THOMSON J. A. (2007) Induced pluripotent stem cells lines derived from human somatic cells. *Science* 318: 1917-1920.

YU, M., WU, P., WIDELITZ, R.B., CHUONG, C.M. (2002). The morphogenesis of feathers. *Nature* 420: 308–312.

YUE, Z., JIANG, T.X., WIDELITZ, R.B., CHUONG, C.M. (2005). Mapping stem cell activities in the feather follicle. *Nature* 438: 1026-1029.

Further Related Reading, published previously in the *Int. J. Dev. Biol.*

See our Special Issue ***Skin Development*** edited by Danielle Dhouailly at:
http://www.ijdb.ehu.es/web/contents.php?vol=48&issue=2-3

See our Special Issue ***Fertilization***, in honor of David L. Garbers and edited by Paul M. Wassarman and Victor D. Vacquier at:
http://www.ijdb.ehu.es/web/contents.php?vol=52&issue=5-6

Analyses of regenerative wave patterns in adult hair follicle populations reveal macro-environmental regulation of stem cell activity
Maksim V. Plikus, Randall B. Widelitz, Rob Maxson and Cheng-Ming Chuong
Int. J. Dev. Biol. in press doi: 10.1387/ijdb.072564mp

Transdifferentiation of corneal epithelium: evidence for a linkage between the segregation of epidermal stem cells and the induction of hair follicles during embryogenesis.
David J Pearton, Corinne Ferraris and Danielle Dhouailly
Int. J. Dev. Biol. (2004) 48: 197-201

How and when the regional competence of chick epidermis is established: feathers vs. scutate and reticulate scales, a problem en route to a solution.
Fabrice Prin and Danielle Dhouailly
Int. J. Dev. Biol. (2004) 48: 137-148

The different steps of skin formation in vertebrates.
Isabel Olivera-Martinez, Jean P Viallet, Frederic Michon, David J Pearton and Danielle Dhouailly
Int. J. Dev. Biol. (2004) 48: 107-115

Ventral vs. dorsal chick dermal progenitor specification.
Ingrid Fliniaux, Jean P Viallet and Danielle Dhouailly
Int. J. Dev. Biol. (2004) 48: 103-106

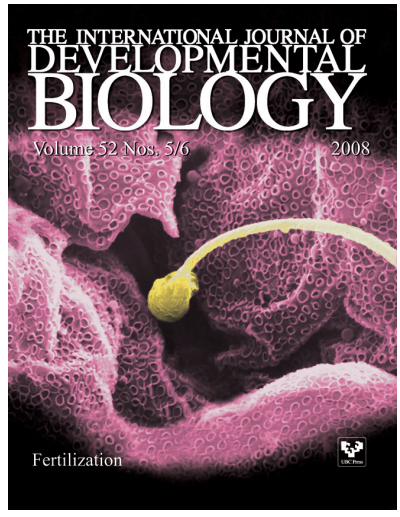
Molecular mechanisms controlling dorsal dermis generation from the somitic dermomyotome.
Isabel Olivera-Martinez, Jacques Thélu and Danielle Dhouailly
Int. J. Dev. Biol. (2004) 48: 93-101

Skin field formation: morphogenetic events.
Danielle Dhouailly, Isabel Olivera-Martinez, Ingrid Fliniaux, Sylvain Missier, Jean P Viallet and Jacques Thélu
Int. J. Dev. Biol. (2004) 48: 85-91

Adult epidermal keratinocytes are endowed with pilosebaceous forming abilities.
C Ferraris, B A Bernard and D Dhouailly
Int. J. Dev. Biol. (1997) 41: 491-498

Characterization of cDNAs encoding two chick retinoic acid receptor alpha isoforms and distribution of retinoic acid receptor alpha, beta and gamma transcripts during chick skin development.
J J Michaille, B Kanzler, S Blanchet, J M Garnier and D Dhouailly
Int. J. Dev. Biol. (1995) 39: 587-596

Differential expression of two different homeobox gene families during mouse tegument morphogenesis.
B Kanzler, J P Viallet, H Le Mouellic, E Boncinelli, D Duboule and D Dhouailly
Int. J. Dev. Biol. (1994) 38: 633-640



5 yr ISI Impact Factor (2008) = 3.271