

**How we can learn more by integrating physics perspective to biology quest:
Stem cells, feather architecture, hair regeneration and avian evolution**

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During biological organization, cells use genomic information to orchestrate chemical and physical processes for the generation of organized tissues and organs. More chemical principles in life sciences have been brought to light than physical principles. We explore the contribution of physical principles in morphogenesis using the integumentary appendages (feathers, hairs, teeth, etc.) as the model for two reasons. First, the integument is more accessible to experimentation and integument appendage stem cells have robust regeneration powers. Second, most of the function of integument organs is based upon their structural architecture (e.g., in contrast to liver which is more a chemical factory), thus allowing us to analyze the biophysical properties of their functional forms.

I will show several examples of this organization in different length scales (cells, tissues, organs and organisms) and different time scales (embryogenesis, growth, regeneration after wounding, and evolution). 1) In the developing skin, de novo periodic patterning leads to the formation of thousands of feather or hair primordia, allowing variations to be generated. The process involves the Turing activator / inhibitor principle, but how the mechanical-chemical process translates chemical patterns into physical structures is not fully understood. Using a reconstitution assay, real time imaging shows dynamic self-organizing behavior and the involvement of physical principles in morphological phase transitions. 2) Mature feathers are made of dead keratinocytes which were mainly made of keratins. Before these feather keratinocytes die, they are organized into different shapes and arrangements, giving feathers a remarkable range of rigidity and flexibility based on the different organization of feather stem cells. The chicken frizzle mutant has a mutation of alpha keratin 75, and exhibits a defective feather rachis medulla and a frizzled feather shape. 3) A single hair follicle undergoes cyclic regeneration. In a population of hair follicles, is their regenerative behavior coupled? We show that when a hair is plucked, it releases stress molecules. After topology-based hair plucking, quorum sensing can be elicited in the collective regenerative behavior. With optimal conditions, we can pluck 200 hairs and get 1000 hairs to be activated. 4) About 150 million years ago, the skin appendage of some dinosaurs start to change their physical structures by elongation, forming branches, vanes, which allow them to gain endothermy, communication and ability to fly, thus the birth of birds.

These are examples where physical principles permeate biological processes. Through multi-disciplinary collaborations, integration of physical perspectives and model simulation can help us reach a more holistic understanding of our biological questions.

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Introduction of Cheng-Ming. Chuong, M.D., Ph.D

Dr. Cheng-Ming Chuong received his M.D. from Taiwan University in 1978. He then obtained his Ph.D. from The Rockefeller University in 1983. Later he moved to the University of Southern California in 1987 and work on the development and regeneration of feather, tooth, and hairs. He is currently a professor of pathology and also serves as the Chair of Graduate Committee in Department of Pathology. Dr. Chuong directs the Laboratory of Tissue Development and Engineering (<http://www-hsc.usc.edu/~cmchuong/> cmchuong@usc.edu) in the Department of Pathology, USC. The laboratory is mainly supported by National Institute of Health and studies how stem cells are guided to form special tissues and organs of specific size and shape.

Dr. Chuong has received many honors including the award for creativity in research by USC. In 2008, he was elected to the prestigious Academia Sinica, the National Academy equivalent of Taiwan. In 2014, he was elected as a fellow of American Association for the Advancement of Science for “Distinguished contribution to advance new understanding in the development, regeneration and evolution of patterns in ectodermal organs”. His work on Evo-Devo of feathers contributes to new understanding in the “The Birth of Birds” which was chosen by Science as one of the 10 major breakthroughs in 2014.

Using the ectoderm as a model, his laboratory learned from nature how to mold stem cells into different ectodermal organs during development, evolution and stem cell engineering. He has promoted the concept of “topobiology” which is crucial for guiding epidermal stem cells into proper architectures. He demonstrated how the process can guide stem cells to the multiple forms of ectodermal organs.

Dr. Chuong has published more than 210 papers on the biology of integuments in top journals, including multiple research papers and commentaries in Nature, Science, CELL. He publishes two books (Molecular Basis of Epithelial Appendage Morphogenesis; Fossil Birds of China) and two journal special issues (Development and Evolution of Amniote Integuments; Pattern Formation). He is an associate editor / editorial board of Scientific Report, J. Investigative Dermatology, Developmental Biology, J. Expt. Zoology, etc.

He wrote chapters for textbooks on stem cell biology and regenerative medicine in English and in Chinese. He is frequently interviewed by the media for his work in stem cell biology and evolution and development of feathers and other integument organs. Interviews have appeared in LA times, BBC, Scientific American, Smithsonian magazine, NPR, Science Daily News, Business week, Chinese Daily news, Fox news, etc.

In Taiwan, he helps establish multi-disciplinary research teams. He collaborates with Integrative Stem Cell Center of China Medical University and also works as honorary director for Center for Developmental Biology and Regenerative Medicine of National Taiwan University, International laboratory of Wound Repair and Regeneration of National Cheng Kung University (iWRR), and Integrative Evolutionary Galliform Genomics (iEGG) Center of National Chung Hsing University.