

從皮毛之道 談幹細胞及演化

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

鍾正明

Department of Pathology,

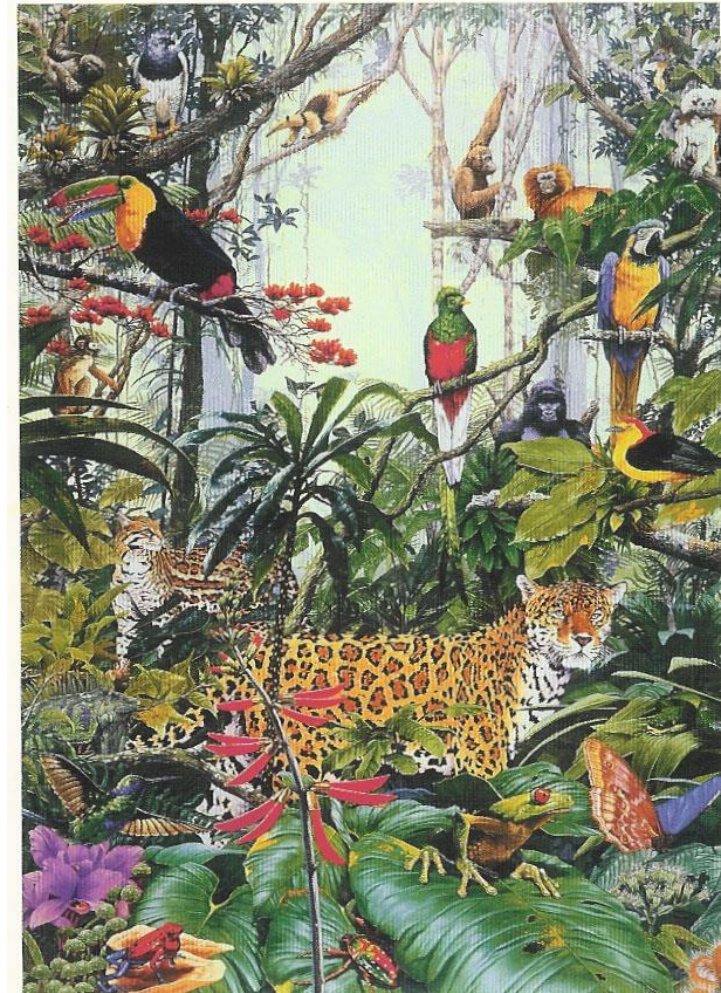
School of Medicine,

University of Southern California,

cmchuong@usc.edu

中央研究院院士

<https://sites.usc.edu/cmchuong/>



Bio-inspired approaches

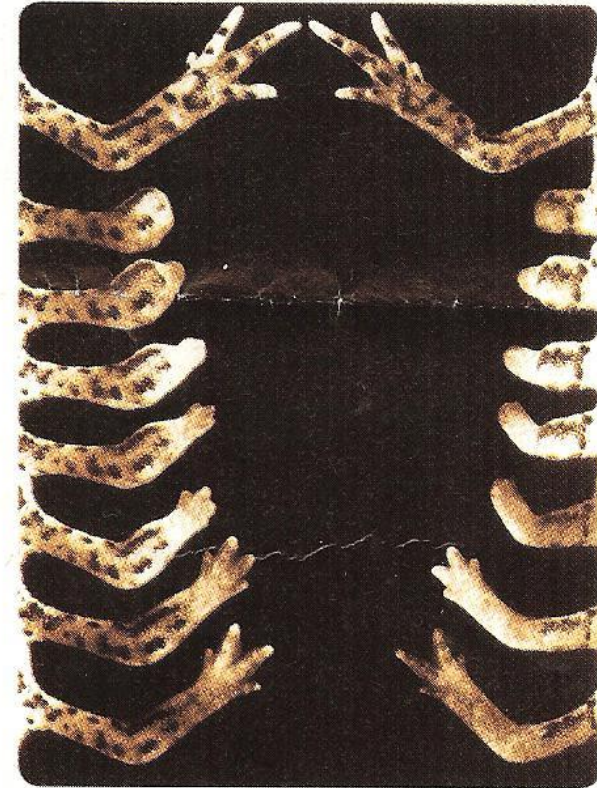
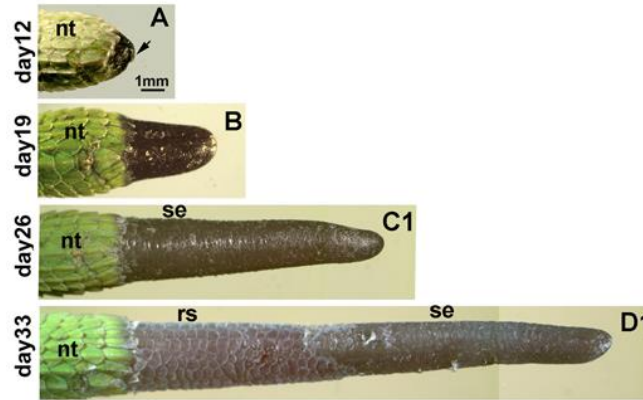
1. Can animals regenerate certain organs?

(再生生物學)



2. How do they regenerate?

(再生之道)



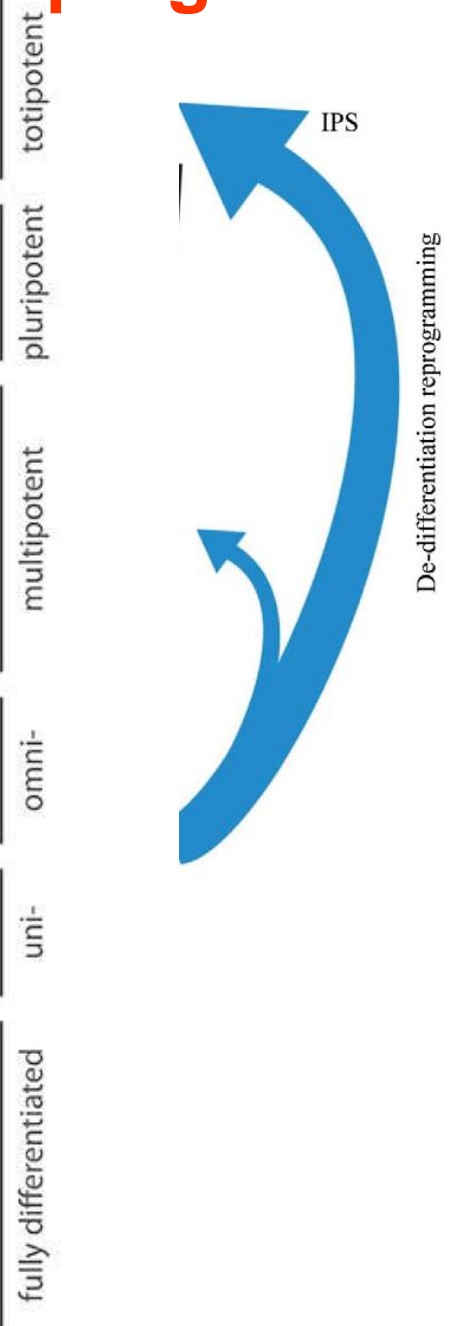
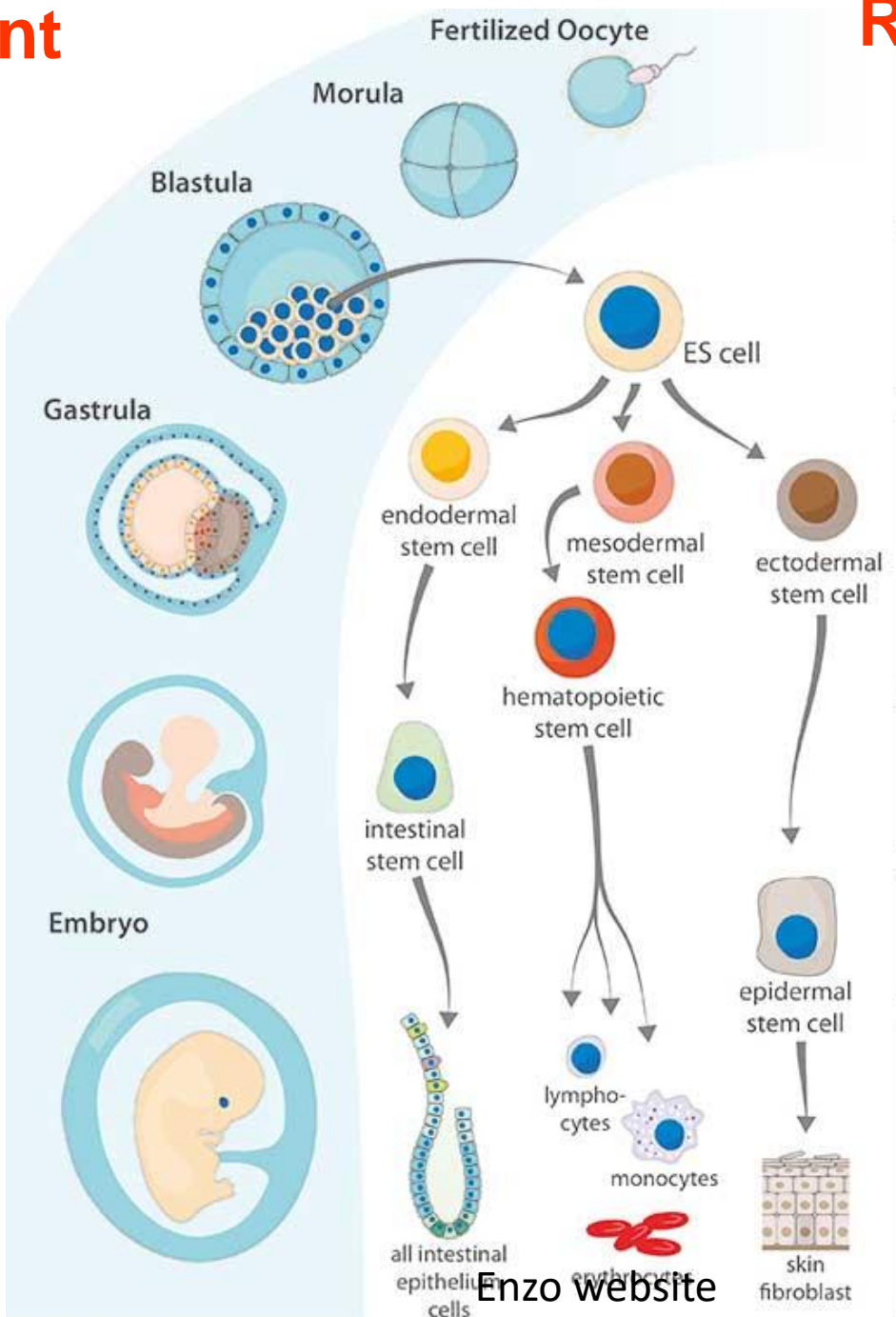
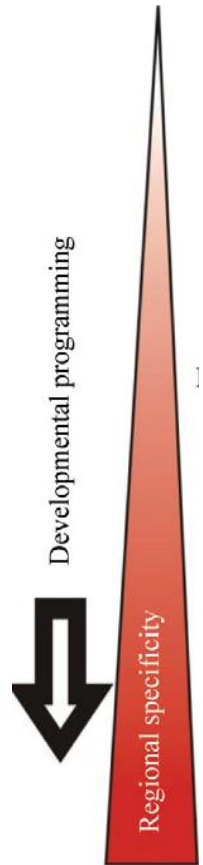
3. Can human learn some of this ability and use it in medicine? (再生醫學)

Outline

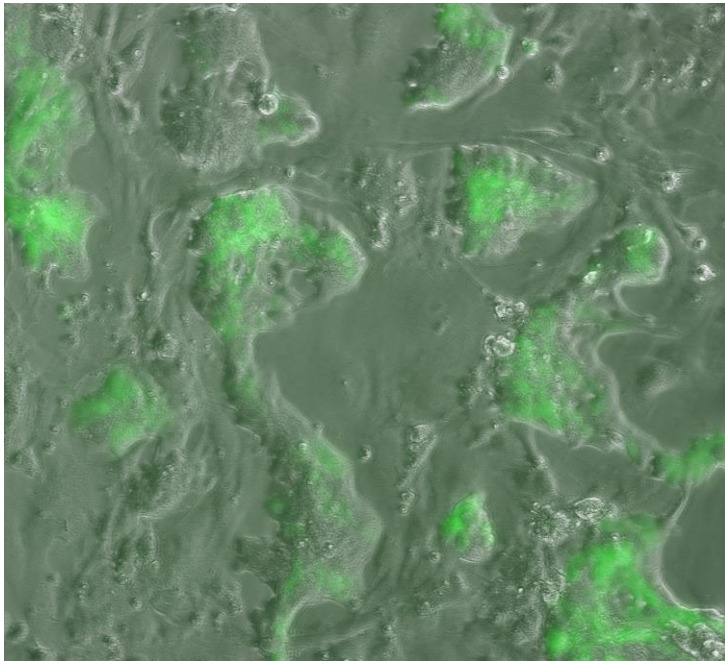
- **Basics:** Development, stem cells, reprogramming
- **Applications:** Wound regeneration and organoids
- **Basic biology:** Hairs and feathers

Development

Reprogramming



Enzo website



Yamanaka ,
Nobel Prize, 2012

- **Sources:**

Embryonic stem cells

iPS (induced pluripotential stem cells)

Adult stem cells

- Residential stem cells,
- Mesenchymal stem cells
- Amniotic fluid ...etc.

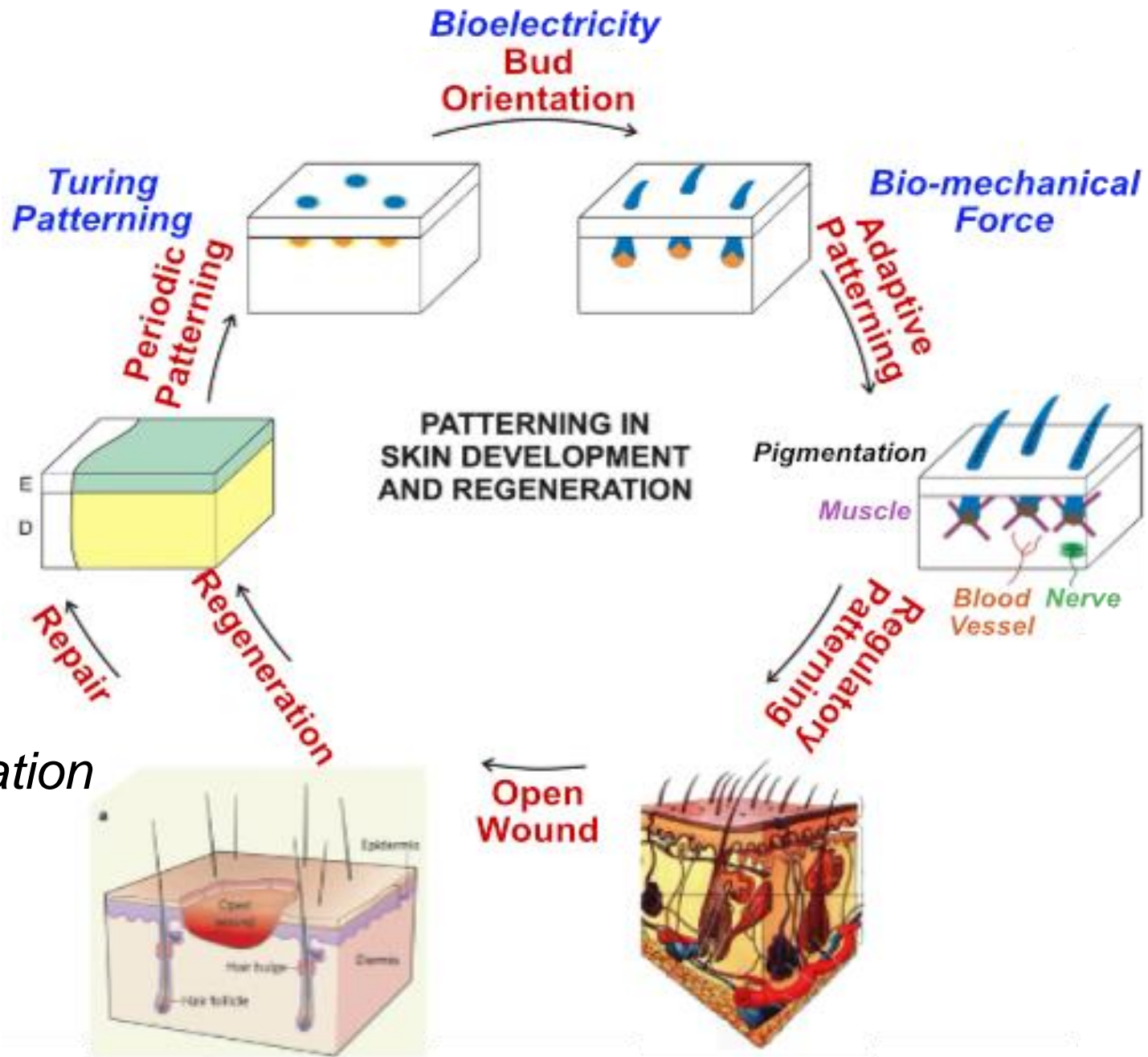
- **Function:**

- self-renewal
- Pluri-potent, multi-potent
- Germ line transmission

Challenges:

Differentiation
Morphogenesis
Regulation

Teratoma
Tissue organization

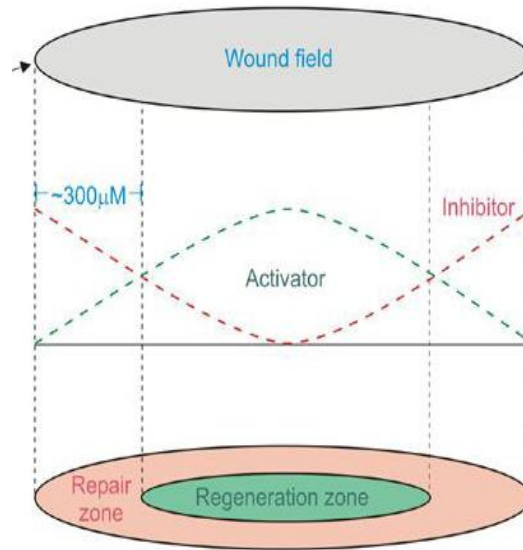
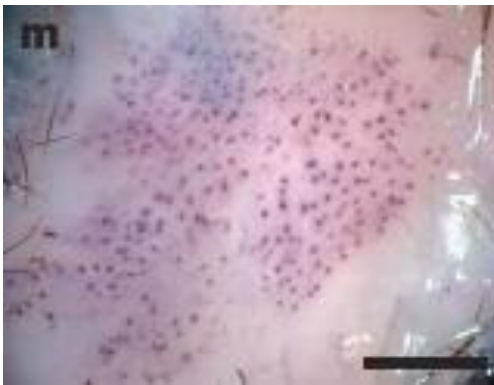


Outline

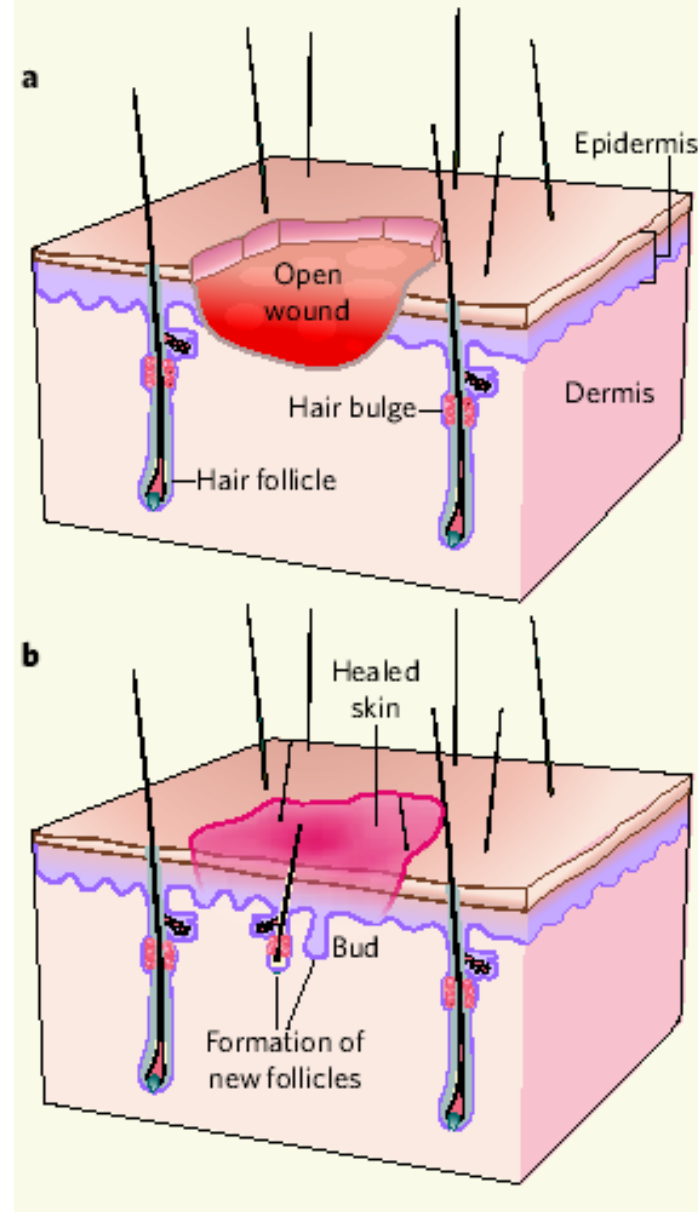
- **Basics:** Development, stem cells, reprogramming
- **Applications:** Wound regeneration and organoids
- **Basic biology:** Hairs and feathers

Wound induced Hair Neogenesis

Endogenous Reprogramming



Regeneration from
the center of wound
bed

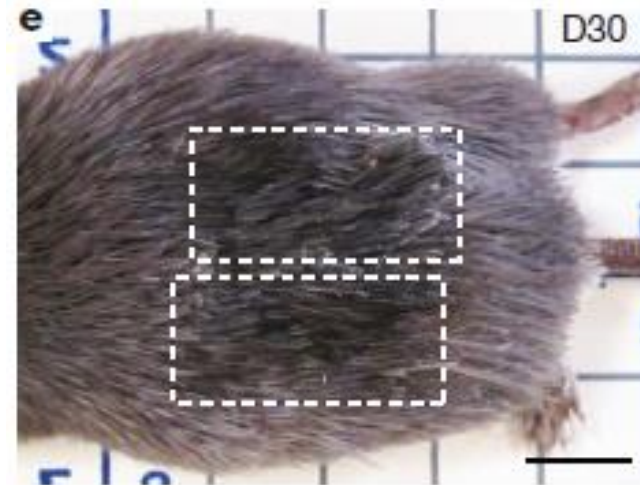
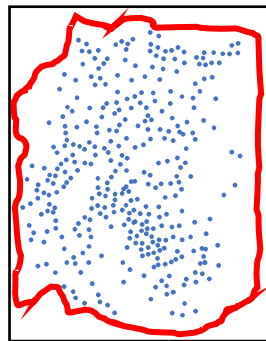
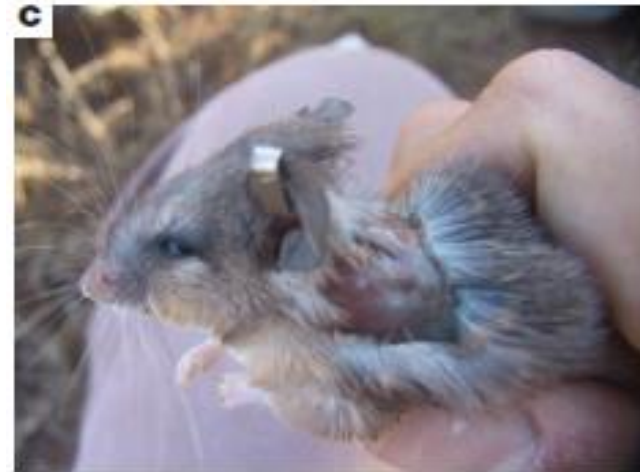


Ito., Cotsarelis. Nature, 2006; Chuong, Nature, 2006

Hughes et al., 2018. J. Invest Dermatol Msx2 KO mice can not undergo WIHN

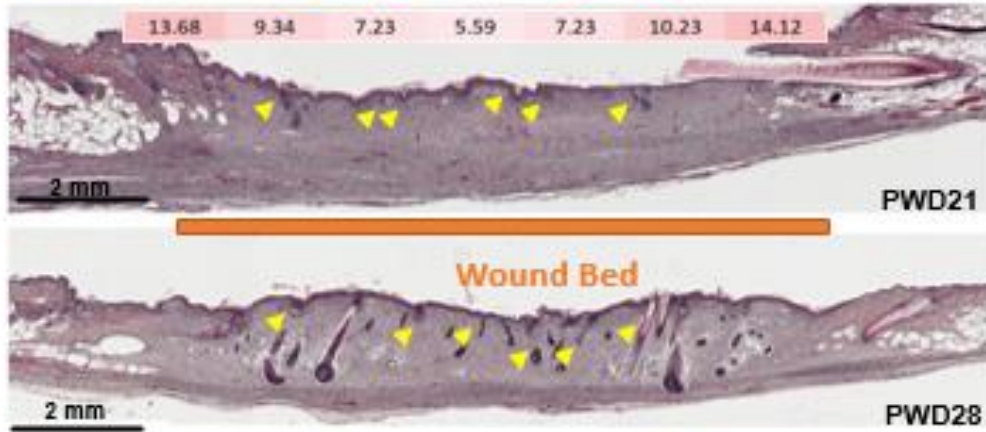
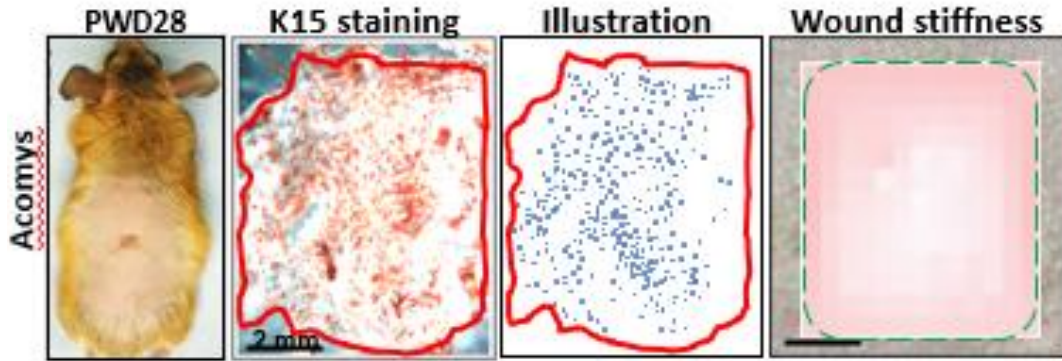
Bio-inspired approaches **Spiny mouse** 非洲刺鼠

Robust Endogenous reprogramming



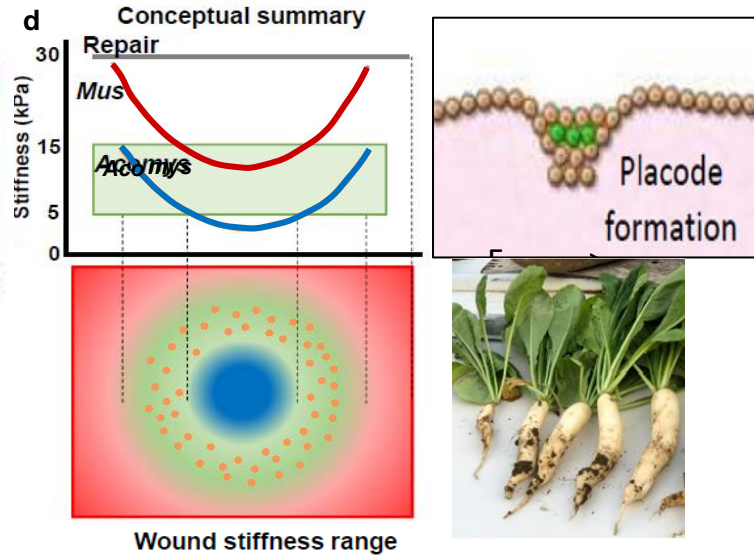
Seifer ..Maden, Nature, 2012
Jiang et al., Expt Derm. 2019;
Harn et al., Nat Comm, 2021

Tissue mechanics modulate the outcome of wound regeneration





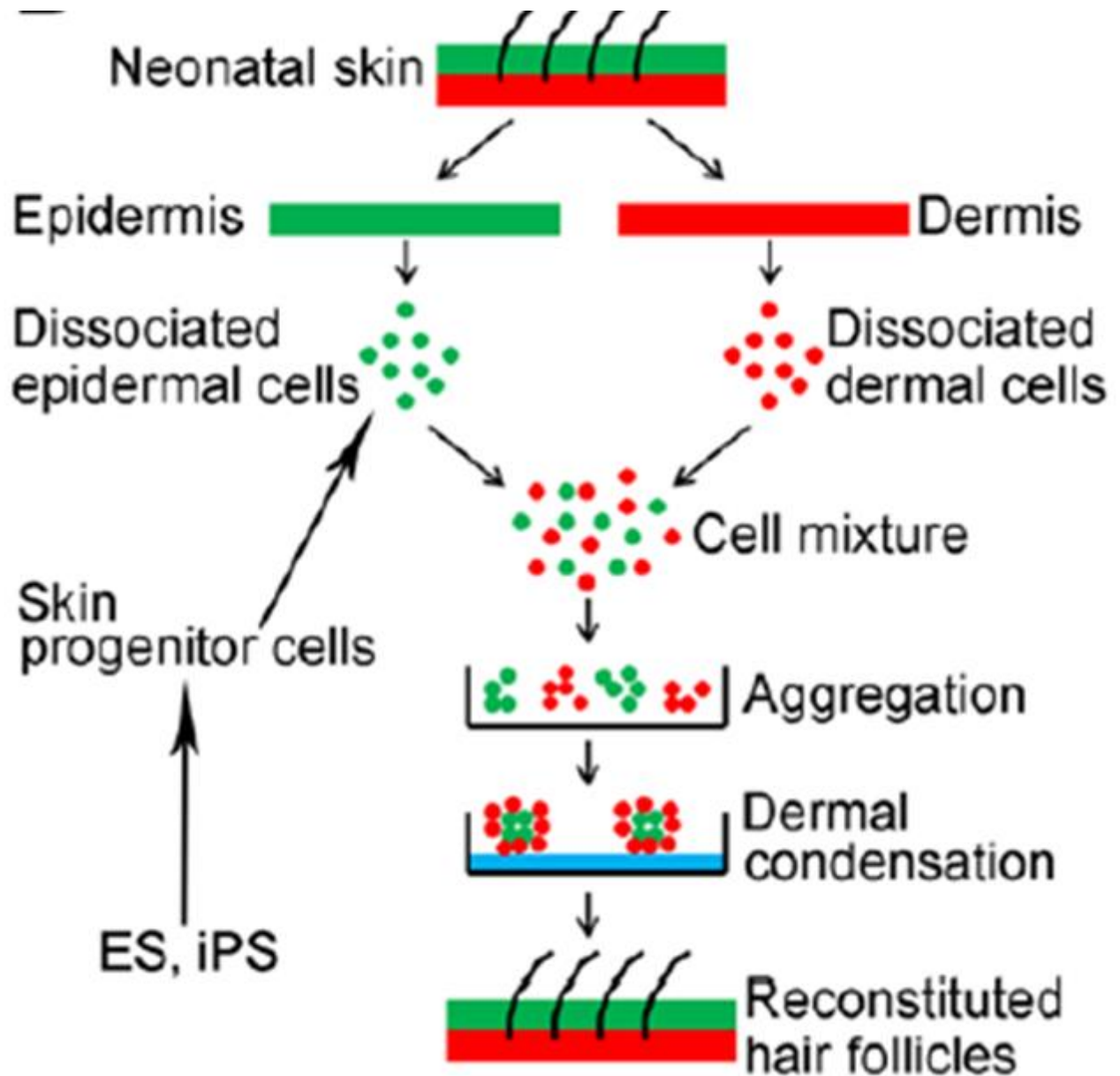
 Hair neogenetic zone
 Propagate from periphery to center



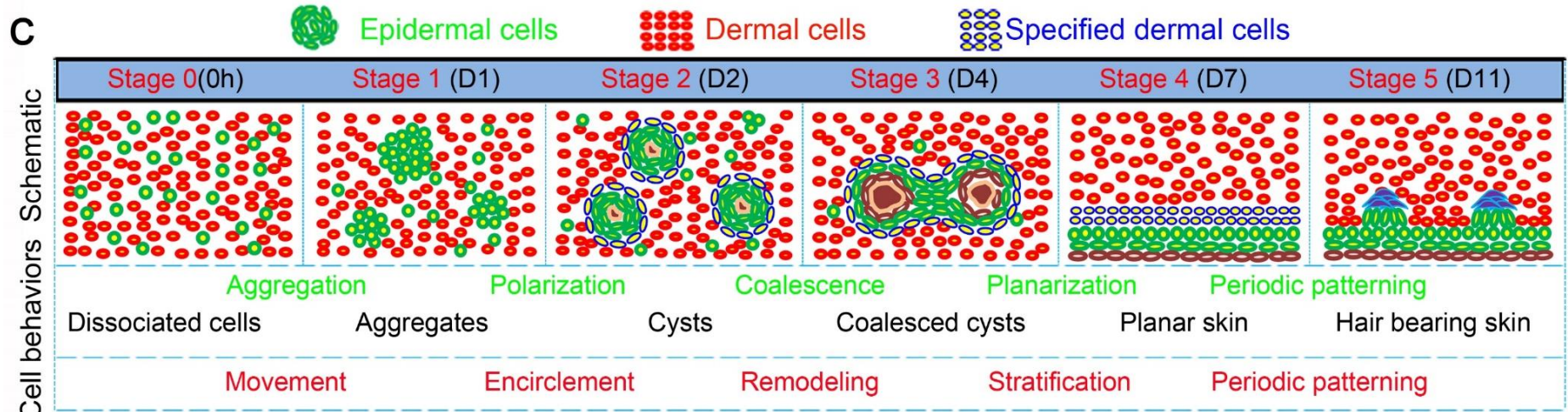
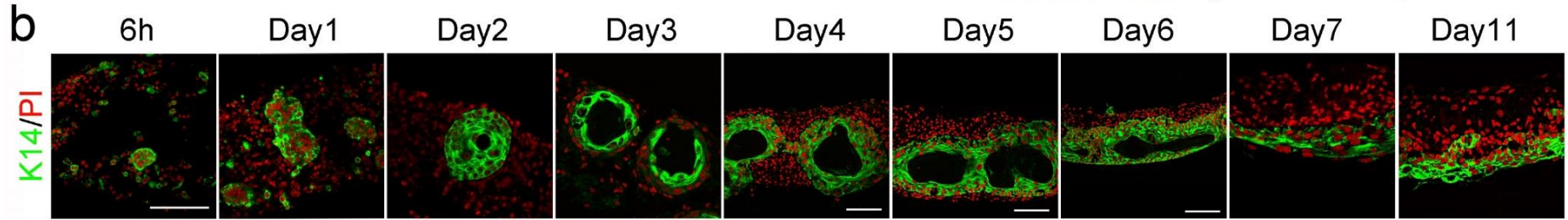
Hans Harn,
 Shen Pei Wang et al.,
 2021, Nat Comm

韓憶航博士,
 王聖斐醫師

Skin Organoids



Self-organizing behavior of skin Organoids



Lei et al., 2017, PNAS

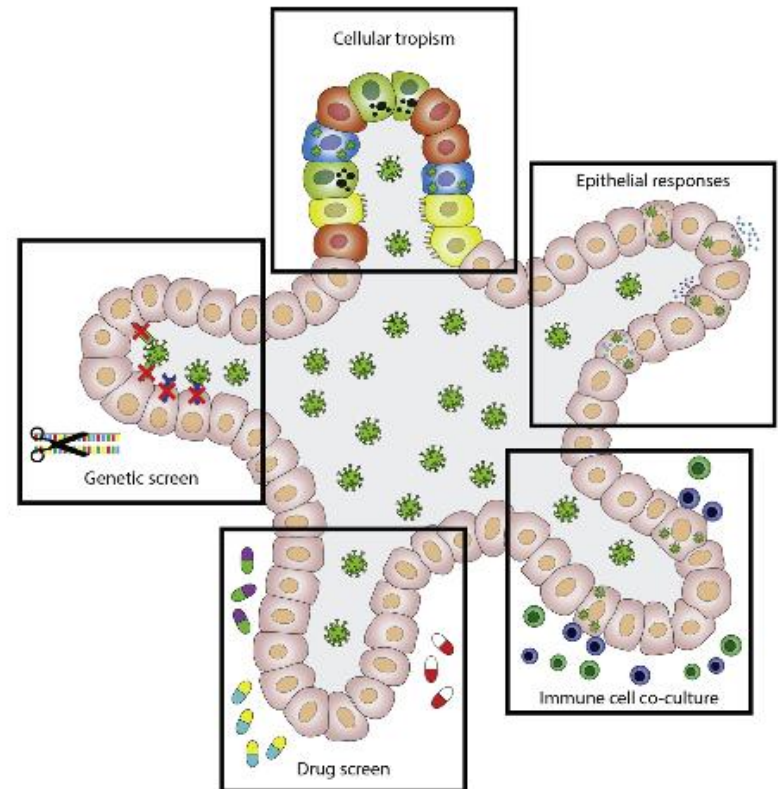
More organoids (類器官)

Hans Clevers and others
Kidney, Brain, Gut, liver, pancreas, etc.

Screening small molecules

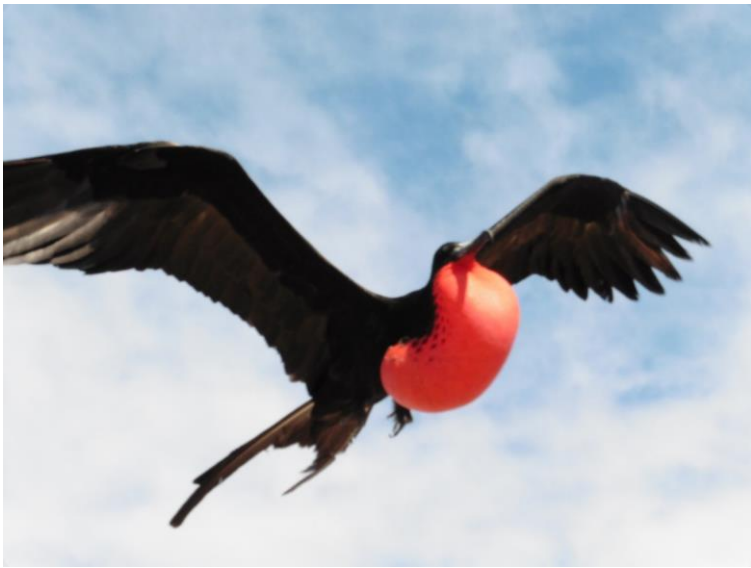
Delivery to patients

Study principles of morphogenesis



Outline

- **Basics:** Development, stem cells, reprogramming
- **Applications:** Wound regeneration and organoids
- **Basic biology:** Hairs and feathers



Frigate Bird,
Galapagos Islands

Arctic fox,



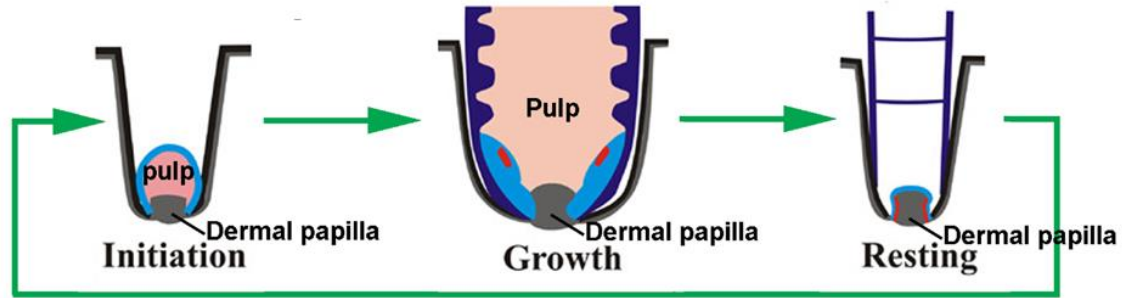
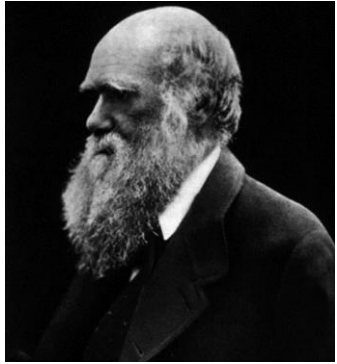
Function of the integuments:

Endothermy,
Locomotion,
Communication

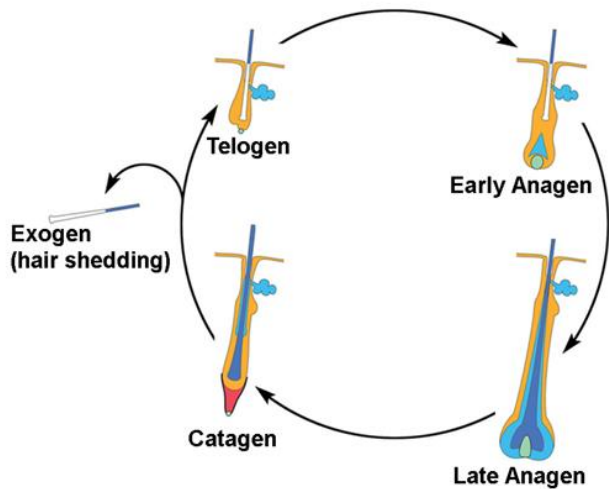
Adaptation to
changing environments



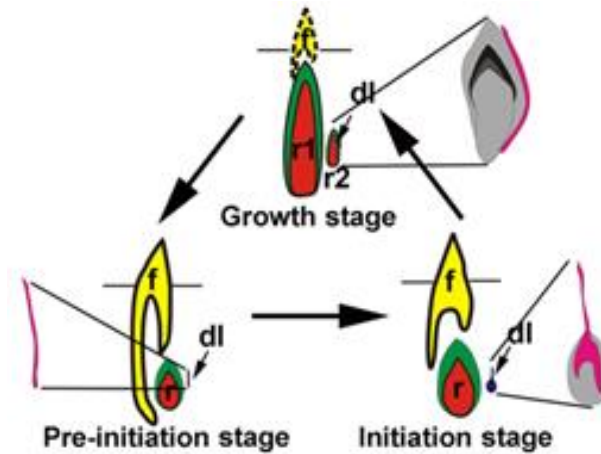
Three kinds of follicles: *Physiological cyclic renewal, stem cell and niches*



The Feather cycle



The Hair cycle



Alligator tooth cycle



Male pattern baldness (雄性秃) Androgenetic alopecia is a stem cell disease.

Region, scalp, beard, eyebrow

Age

Sex, male: region; female: diffuse



In early stages, stem cells are nearly normal,
but can not be activated by the environment.

南極仙翁

Current ways of hair restoration

Hair follicles and the environment
Improving Soil, obtain stem cells,

Hair transplantation

Minoxidil (Rogaine): potassium channel opener

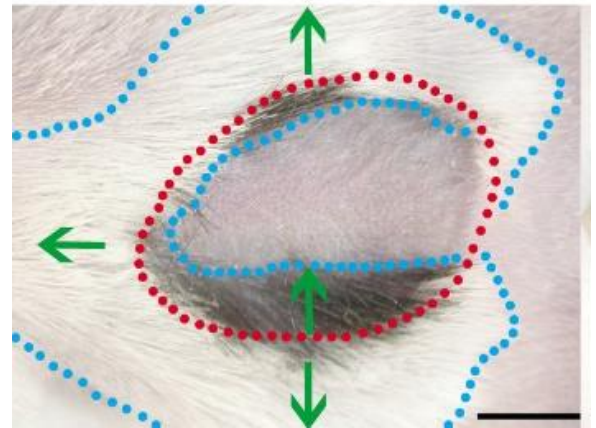
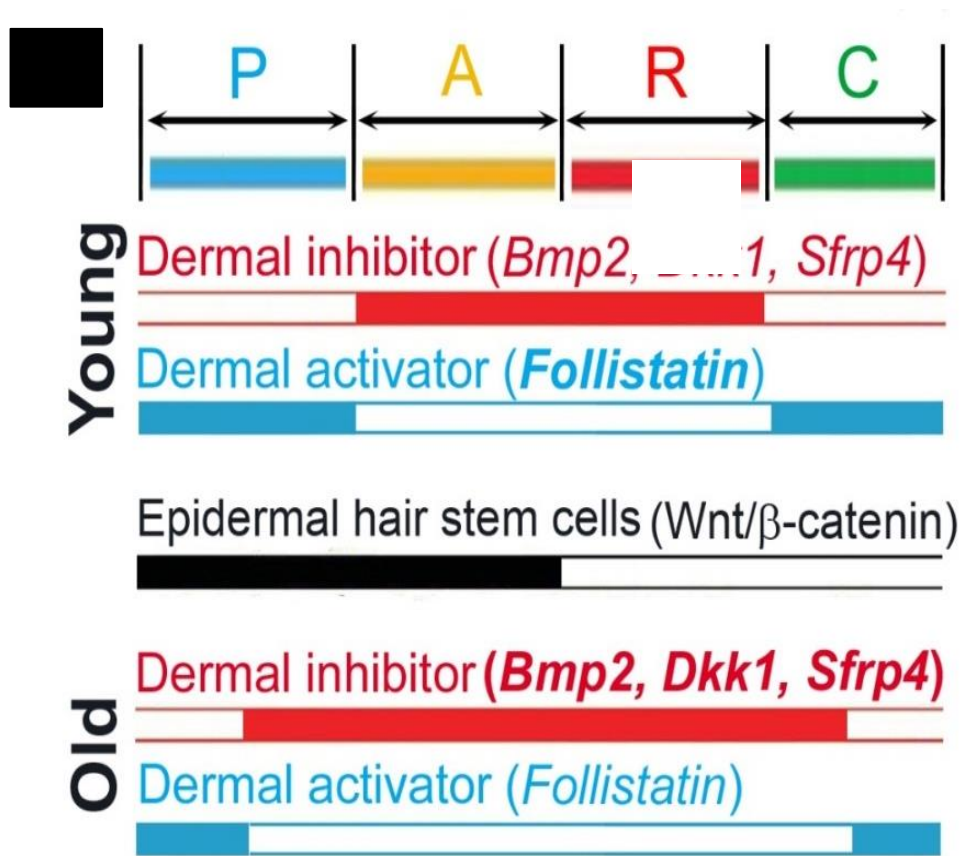
Finasteride (Proscar): 5 alpha reductase inhibitor

Prostaglandin D2 inhibitor

Activate Stem cells

Deliver “Stem cells”

Aging: Changes of stem cells or local environment?



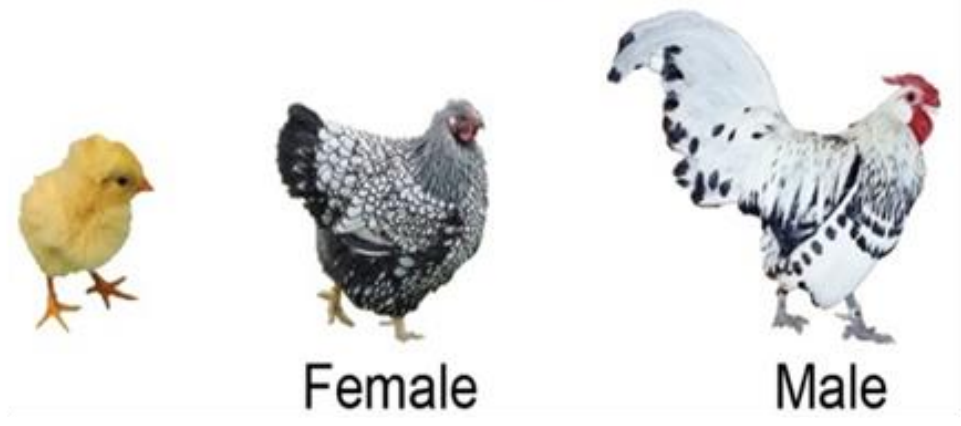
Old mouse hair regeneration can be rescued when the skin is transplanted to young mouse

Chen et al., 2014, JID.

Hair changes during the life cycles of human beings & *Cervus elaphus*



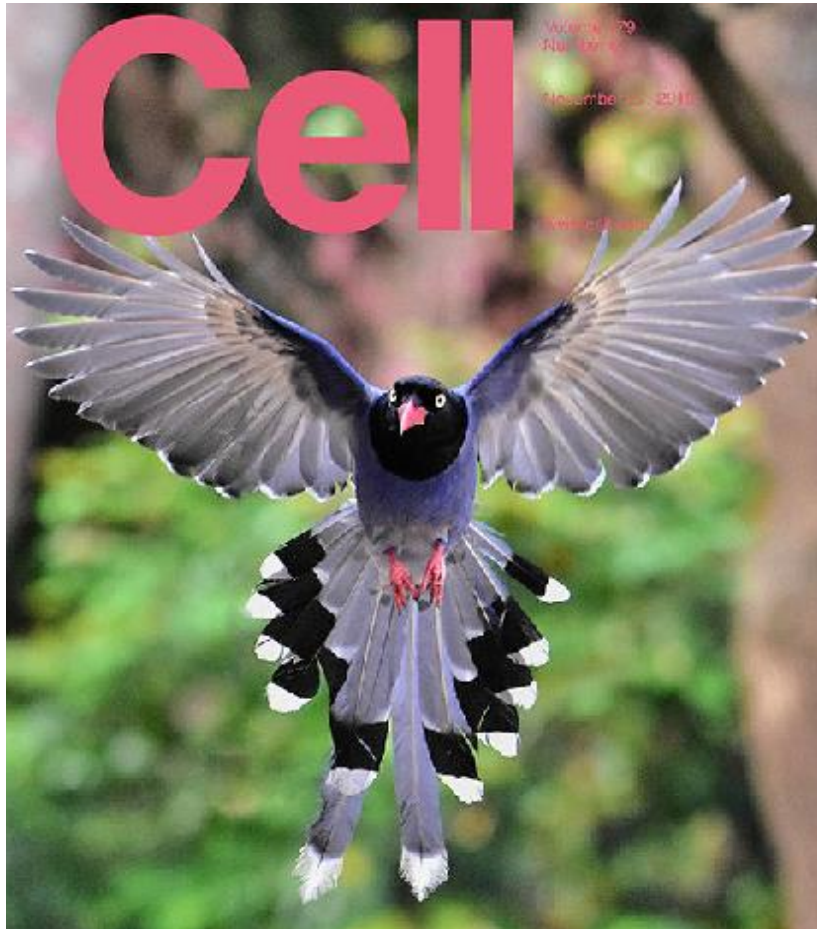
Baby Puberty Reproductive stage Ageing Death



Regional differences

Temporal differences

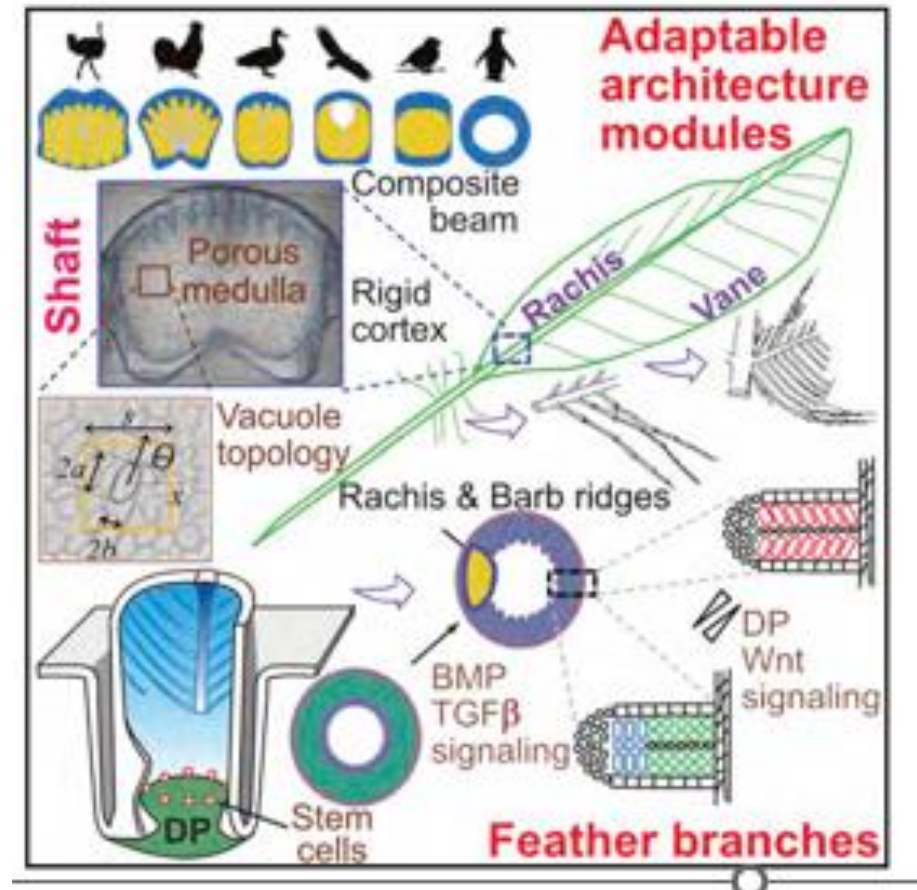
The Making of a Flight Feather: Bio-architectural Principles and Adaptation



台灣藍鵲

Taiwan Blue Magpie (national bird of Taiwan)

Photo by Mr. Shao Hua Lang



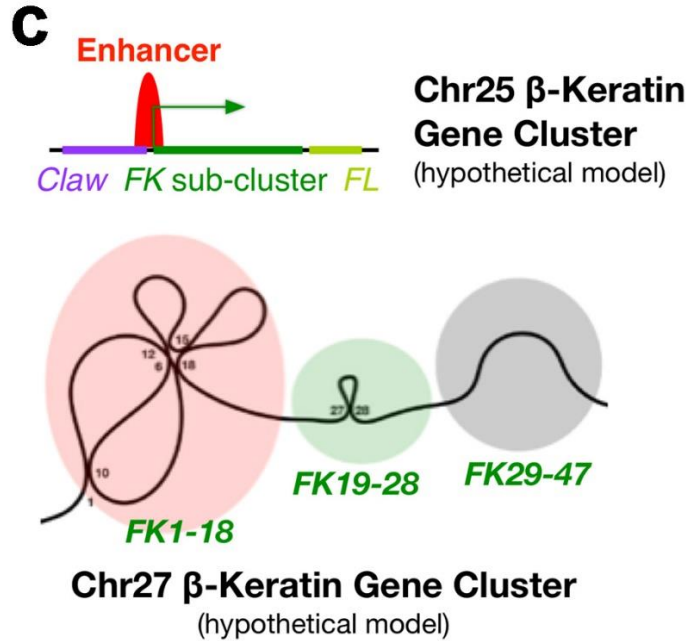
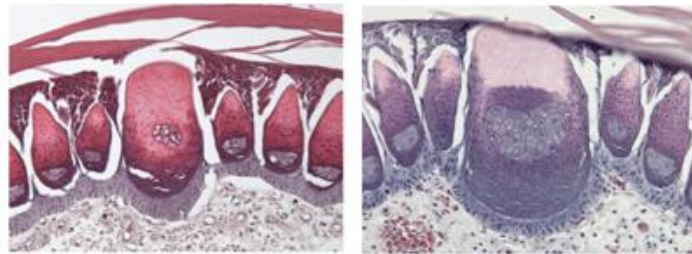
Wei-Ling Chang, Hao Wu,
Yu-Kun Chiu, ..., Ping Wu, Wen-Tau Juan,
Cheng-Ming Chuong

Collaboration with China Medical University



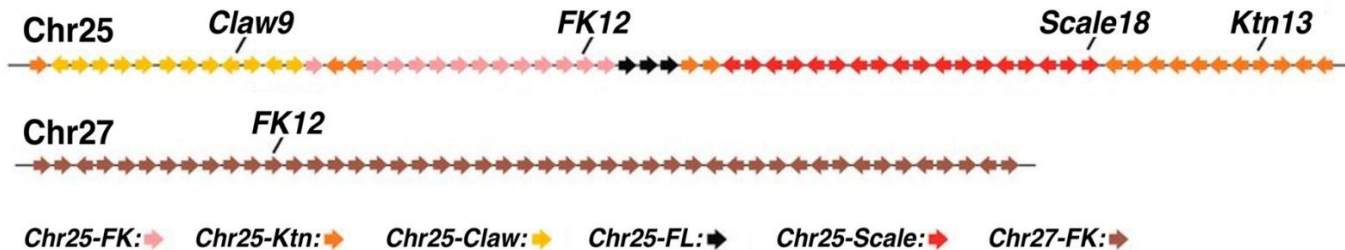
Frizzle chicken 捲毛雞, 鳳梨雞

Mutation in keratin 75



WH Li
李文雄院士
Gene Ng
Academia Sinica
中央研究院

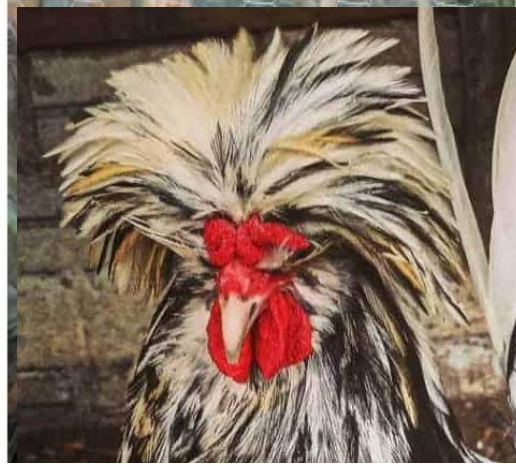
b β -Keratin Gene Clusters



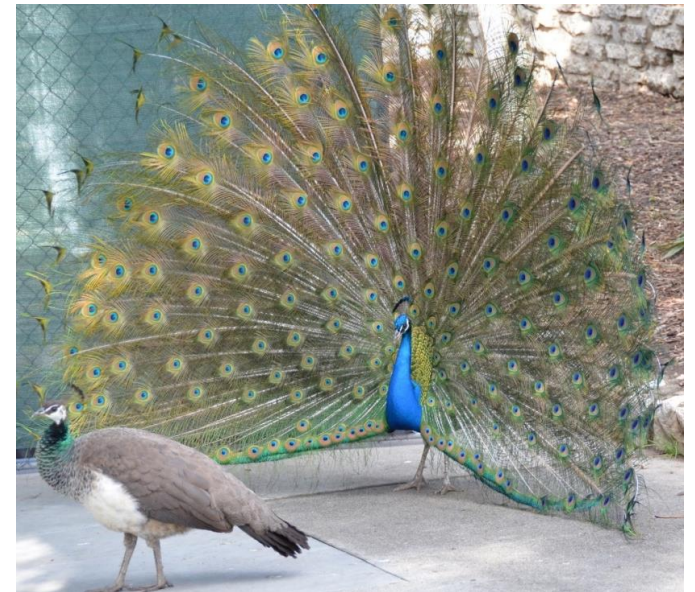
Wild-type:
White Leghorn



Crested:
White Crest Black Polish

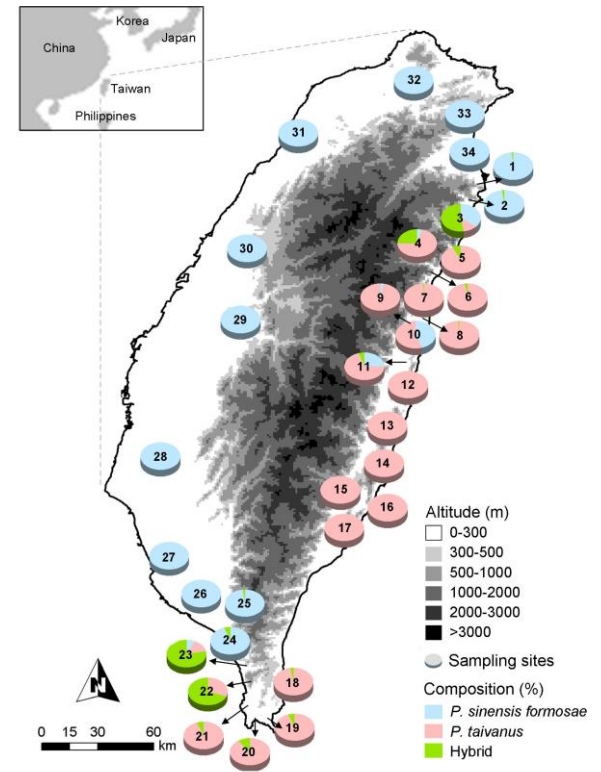


Bearded:
Huiyang Bearded chicken



Darwin: Survival of the fittest, Sexual selection.

烏頭翁, 白頭翁, Bulbul



Population distribution,
Hybrid zone

Speciation



于宏燦
姚正得
唐品琦
張芳嘉,

The colors of budgeries:







WT

blue mutant



Psittacofulvin pigmentation
+ -

Structural color	+		
	-		

(Yellow pigment + blue structural color = green appearance)



Genome-wide mapping of *blue* trait



R/W amino acid change in polyketide synthase

Structural color: blue
Chemical color: yellow



Cooke, Stanford Univ

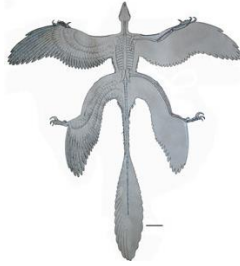
BREAKTHROUGH OF THE YEAR (2014) : The Birth of Birds

REVIEW SUMMARY

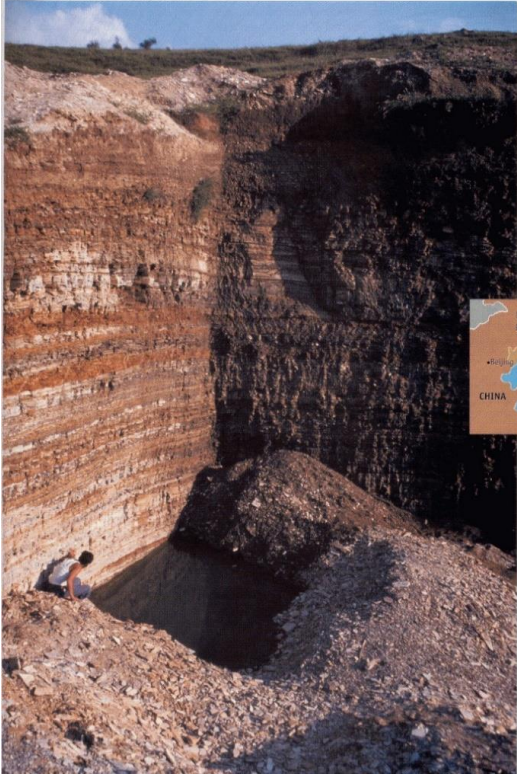
Science 2014

AVIAN EVOLUTION

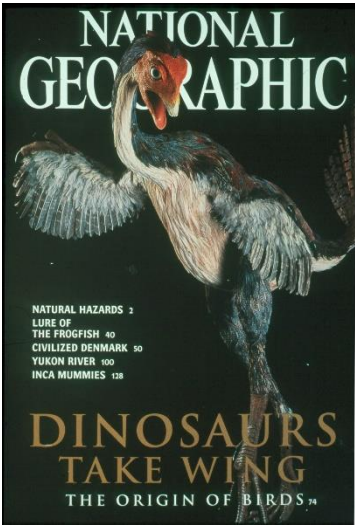
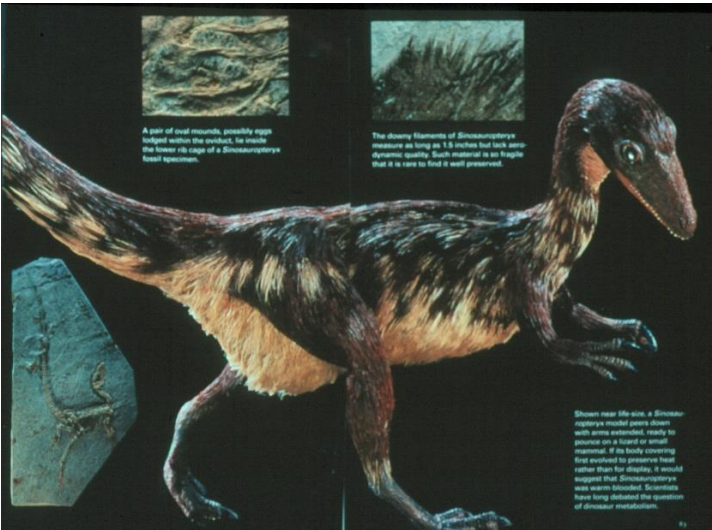
An integrative approach to understanding bird origins



Xing Xu, Zhonghe Zhou, Robert Dudley, Susan Mackem, Cheng-Ming Chuong, Gregory M. Erickson, David J. Varricchio



Beneath the green farm country of Liaoning, northeast of Beijing, layers of sediment preserve communities of organisms that lived in and near ancient lakes: plants, insects, small dinosaurs, birds, fish, various reptiles, and mammals.



Jehol Biota,
~ 120-130 million years ago

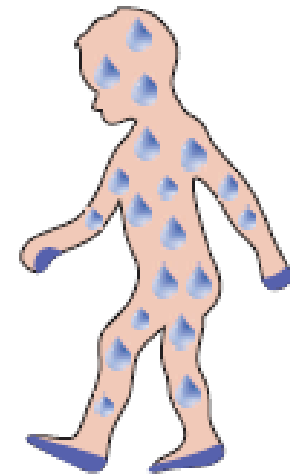
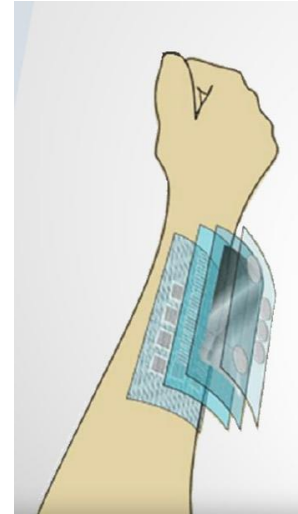
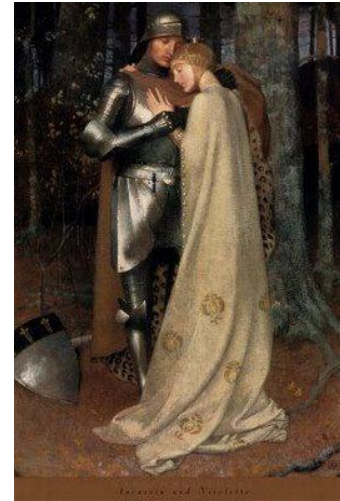
Integuments in human evolution

Intelligent skin

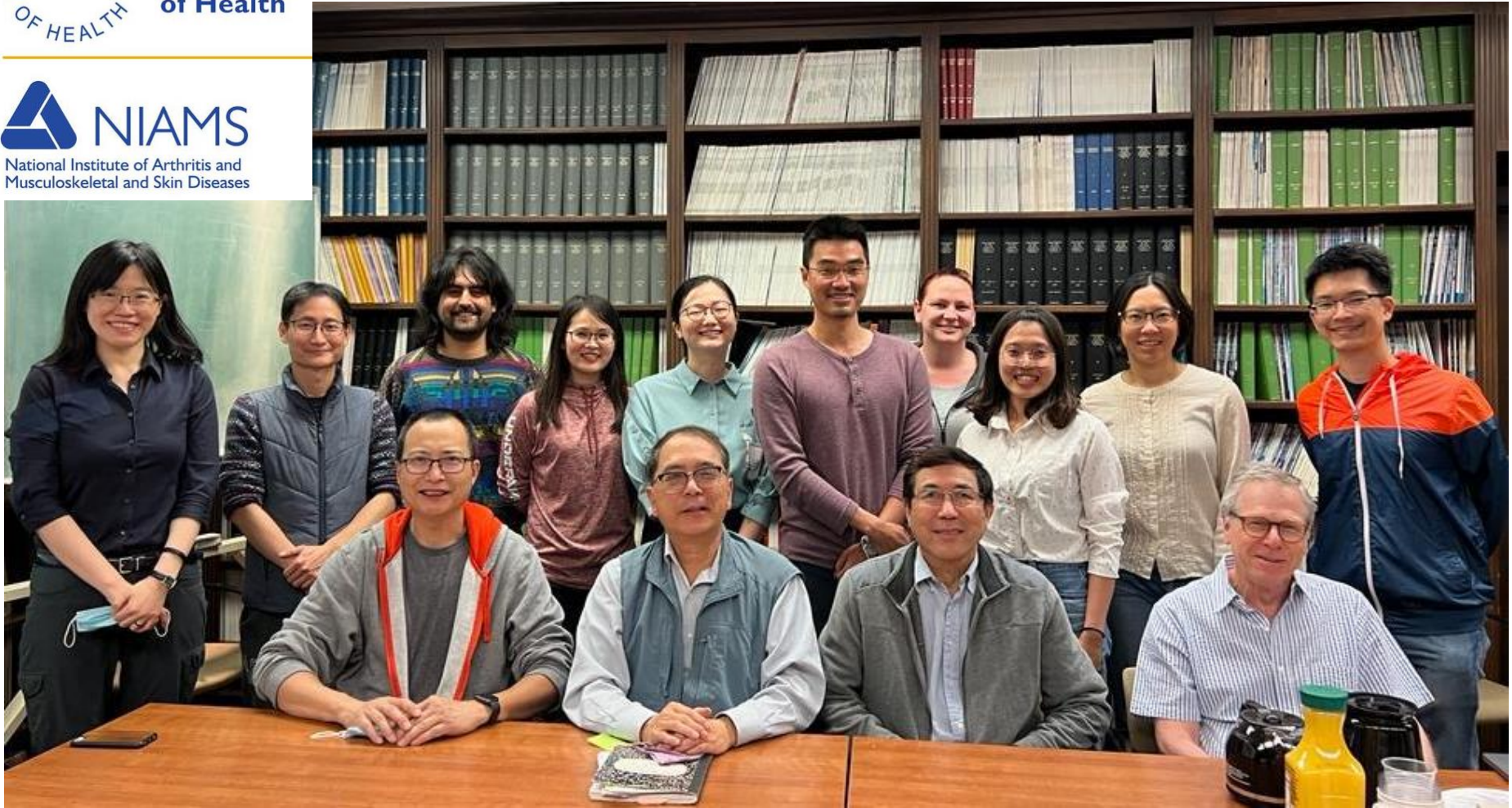
The making of a face
sweat gland In the trunk



Paabo
Nobel
Prize,
2022



Supported by the



[Chuong Lab: cmchuong@usc.edu](mailto:cmchuong@usc.edu)

<https://sites.usc.edu/cmchuong/>

https://en.wikipedia.org/wiki/Cheng-Ming_Chuong

Acknowledgement

University of Southern California
cmchuong@usc.edu (recruiting)
<https://sites.usc.edu/cmchuong/>

Funding:

US:



Taiwan: 科技部, 教育部, 千里馬,
龍門

CMU / USC Collaborative contract
Human Frontier Science Program

Collaborators

*Oxford: P. Maini, R Baker, T Woolley
UC Irvine, A Lander, N Qing,
Sweden, L Andersson
China Medical University
WT Juan*

Taiwan alliance

Academia Sinica

China Medical Univ:

Integrative Stem Cell Center.

National Cheng Kung Univ: iWRR

Int. Wound Repair/Regeneration Ctr

National Taiwan University

National Chung Hsing Univ: iEGG

Int Evolutionary galliform genomics

Taipei Medical Univ

National Defense University

Taipei VA Hospital

科技部, 陳嘉元, 張揚展