



## Pulse kinetics of ERK MAPK controls epidermal stem cell states

**Toru Hiratsuka, M.D., Ph.D.**

King's College London, Centre for Stem Cells and Regenerative Medicine

**Date and Time : 15<sup>th</sup> Apr. 2019 ~~16:00~~~ 16:30~**  
**Place : Yamate Large Meeting Room, 2F Bld. 3**

※The starting time has been changed to 16:30.

Multiple cellular signals fluctuate during development of many organisms; however, the role of signal fluctuation in stem cell fate is unknown in adult human tissues. Here we show in human and mouse epidermal cells that Extracellular-regulated kinase (ERK) changes its pulse kinetics during stem cell state transitions. Proliferative cells showed highly pulsatile ERK activity among stem cell population. Downregulation of both mean and pulse levels caused expression of terminal differentiation marker, Involucrin. We found Meanhi-Pulse profile in slow-cycling stem cells are maintained by  $\beta$ 1-integrin signal. ERK pulse and mean level were independently downregulated by different phosphatase members during differentiation. We observed spatial segregation of human keratinocytes with different ERK pulse and mean profiles on substrates mimicking human dermis. In vivo imaging revealed mouse epidermal cells in the stem cell layer exhibits highly pulsatile ERK patterns compared to differentiated layer cells. Our findings provide a previously-unrecognized mechanism, where pulsatile signal activity underlies stem cell fate control. Our results emphasizes that mammalian tissues are maintained not only by baseline signal activity but also by temporal signal kinetics.

Seminar Language: English

Contact: Aoki (Quantitative Biology Group)