TIFR Centre for Interdisciplinary Sciences
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Seminar

A molecular switch from a single mRNA controls skin homeostasis in wound healing and cancer

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Upon cutaneous injury, keratinocytes at the wound edge transit from quiescent state in normal skin to hyper-proliferation and migration. Many parallels can be drawn between a healing wound and cancer since tumorigenic keratinocytes exhibit hyperplasia and dermal migration/invasion. We have earlier identified a post transcriptional switch controlling keratinocyte migration during wound healing. Expression of microRNA-198 (miR-198) encoded within the 3'-untranslated region (UTR) of follistatin like-1 (FSTL1) gene in healthy epidermis switches to FSTL1 protein synthesis upon wounding. Surprisingly, miR-198 restricts cell migration whereas FSTL1 protein is essential for keratinocytes to initiate migration and wound closure. Switching between these two fate decisions is regulated by KH-type splice regulatory protein (KHSRP) which promotes miR-198 synthesis from FSTL1 transcript. Given the stringent nature of this switch in controlling cell migration, we have found two pathological skin conditions with deregulated switch directly correlating with cell migration status. In chronic diabetic ulcer wounds, miR-198 is turned on persistently, leading to lack of keratinocyte migration and wound repair. On the other hand, cutaneous squamous cell carcinomas (SCCs) hijack this switch by turning on aberrant FSTL1 protein expression to promote the dermal migration/invasion of cancer cells. High levels of miR-181a in SCC, targets and suppresses KHSRP expression, leading to the inhibition of miR-198 synthesis and concomitant FSTL1 expression. Taken together, the stringent control of miR-198/FSTL1 expression appears to be critical for skin homeostasis and deregulation of a single molecular switch can lead to multiple pathologies in skin.

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11:30 AM (Tea/Coffee at 11:15 AM)

Seminar Hall, TCIS