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Keywords: [VCSCB](#) [SPRING](#) [seminars](#)

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Meeting Details

Start Date / Time	April 24, 2019 at 9:00 AM
End Date / Time	April 24, 2019 at 10:00 AM
Duration	1 hour(s)
Location	9455 MRB IV
Presenter Name	Lindsey Seldin, Ph.D. (Macara Lab)
Presentation Title	Non-autonomous induction of epithelial lineage infidelity and hyperplasia by DNA damage
Status	This meeting has already occurred

Meeting Agenda/Notes

Several epithelial tissues, including hair follicles, intestine and lung, contain stem cell reserves to replenish cells lost during normal homeostasis or upon injury. However, how epithelial tissues respond to distinct types of damage, and how stem cell plasticity and proliferation are regulated in these contexts, remain poorly understood. Here, we reveal that DNA damaging agents, but not mechanical damage, induce hyperplasia and lineage infidelity in three related epithelial tissues: the mammary gland, interfollicular epidermis and hair follicle. In the mammary gland, which lacks a bona fide stem cell compartment, we find that DNA damage induces multipotency within the myoepithelial population and hyperproliferation of their luminal progeny, resulting in tissue disorganization. Furthermore, in epidermal and hair follicle epithelia, DNA damage induces basal cell hyperplasia with the formation of abnormal, multi-layered K14+/K10+ cells. This epidermal response does not involve apoptosis or immunity, is epithelial cell non-autonomous, and is induced by stromal fibroblasts. Additionally, epithelial YAP/TAZ become activated, resulting in hyperproliferation. Thus, DNA damaging agents, which are used chemotherapeutically to promote cancer cell death, paradoxically have the opposite effect on wild-type epithelial tissue, promoting stemness, lineage infidelity, and hyperplasia. This work underscores the remarkable plasticity of epithelial cell states and provides mechanistic insight into how normal epithelial behavior can be reprogrammed by DNA damaging agents.

Attachment

 [Fall_2018_Email_Notice_Seldin.pdf](#) - Added on April 19, 2019 at 11:29 AM by Pam Uttz