Q & A

owing questions raised during the above session were answered by Kathy Green. For further information, be contacted at kgreen@northwestern.edu

Q: Daniel Kaufman
Why does psoriasis not blister if it is similar to desmoglein knockout?

Although we see a significant decrease in desmoglein 1 (Dsg1) protein expression in psoriasis, along with other proteins such as connexin 43 whose expression is dependent on Dsg1, this loss is patchy throughout lesional tissue. Importantly, the classic cadherin, E-cadherin, is not lost in these same areas. Further, loss of Dsg1 is not a primary cause of psoriasis and there are many other cell-cell adhesion molecules present in lesional tissue to maintain adhesion. However, we are interested in the possibility that the observed decrease in Dsg1 we see in psoriasis patient tissue could contribute to down-stream effects on cytokine production and disease-relevant signaling.

Q: Marwah Saleh
Does this mean that psoriasis and atopic dermatitis patients have reduced DSG1?

Similar to the answer for the question above, yes, we actually do see a reduction in Dsg1 in psoriasis in patient samples tested so far. Determining the extent to which Dsg1 is reduced (or not) in atopic dermatitis and other ichthyoses will be interesting to address.

Q: Caterina Missero
I wonder if in your latter work on the SAM syndrome you have been able to see TSLP expression in patients' skin?

We have not yet looked for TSLP protein in skin of patients with SAM syndrome. We will be testing for a number of cytokines and junctional proteins before and after drug treatment in these patients.

Q: Hisham Bazzi
Speaking of evolution at the microscale, is DSG1 expressed in the periderm and does its loss affect periderm formation?

We are very interested in periderm formation! Dsg1 comes on right around the time the periderm begins to form, as does Tctex, the dynein light chain that is required to get Dsg1 to the right place on the membrane for delamination to occur in vitro (see: Nat Commun. 2018 Mar 13;9(1):1053). So we are gearing up to look at embryonic stages E9-14, during which time we would normally expect periderm to form, to determine whether loss of Dsg1 results in a delay or impairment of periderm formation.

Q: Kiarash Khosrotehrani
Would you predict that forced expression of DSG1 would reduce UV induced epidermal proliferation and inflammation?

This is an interesting question. We previously demonstrated that forced expression of Dsg1 in UV-treated 3D reconstructed epidermis (raft cultures), increased the kinetics of recovery of those cultures, as assessed by examining markers of keratinocyte differentiation (J Invest Dermatol. 2014 Aug;134(8):2154-2162.) Therefore, it is plausible that forced expression of Dsg1 would reduce UV-induced proliferation and inflammation in vivo.

Q: Declan Lunny
Did you get a chance to look at Dsg1 implicated role in Baretts disease?

No, we have not personally looked at Dsg1 in Barretts esophagus, but loss of Dsg1 does occur in eosinophilic esophagitis and has been implicated in disease pathogenesis. Upon doing a pubmed search, it appears that Dsg1 expression is also affected in Barrett's, so this question deserves further attention.