Treatment of actinic keratosis and squamous cell carcinoma in situ

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Problem
Squamous cell carcinoma is primarily caused by cumulative exposure to ultraviolet (UV) radiation over the course of life. There are approximately 700,000 new people in the United States annually with the incidence of disease increasing up to 200 percent in the past three decades. This number is only projected to increase with aging populations, climate change and breakdown of the ozone layer, which further increases our exposure to UV radiation. Currently, treatments for actinic keratosis and squamous cell carcinoma in situ, precursors to squamous cell carcinoma, include (i) in office procedures (cryotherapy, curettage, photodynamic therapy, laser resurfacing, chemical peel); (ii) prescription medicine that can be used at home (5-fluorouracil (5-FU) cream, diclofenac sodium gel, imiquimod cream, ingenol mebutate gel). 5-FU, imiquimod and ingenol mebutate irritate skin when applied. Diclofenac has lower efficacy than the irritating treatments.

Solution
Seykora and colleagues have demonstrated that topical application of commercially available small molecule kinase inhibitors to SRC kinases and downstream kinases, which are hyperactivated in tissue samples from human patients, provide efficacious targeted and localized therapy for actinic keratosis and squamous cell carcinoma in situ, precursors of squamous cell carcinoma, without inducing inflammation or crusting of skin.

Advantages
- Targeted therapy which inhibits the molecule driving cancer growth. This approach manifests strong potential to reduce irritation associated with the less specific agents that are currently available.
- Preventive and may eliminate damaged cells in UV-exposed skin.
- Many small molecule kinase inhibitors have physico-chemical properties to penetrate skin efficiently.

Immunohistochemical detection of activated SFKs in AKs, and SCISs

Sections of actinic keratoses (AK) and squamous cell carcinoma in situ (SCIS) were incubated with pY416 antibody to detect activated SFKs. Greater degree of membrane and cytoplasmic staining was observed in the AK, and SCIS compared to the unremarkable epidermis. 2 magnifications of representative biopsies are shown.