KEY WORDS: Photoaging, skin cancer, micro-surgery, in-vivo labeling

At current there is no easily accessible molecular indicator of the level of skin UV damage and photoaging correlating with the development of skin cancer. Many known changes, such as the overexpression of matrix metalloproteinases (MMPs), occur only after very prolonged UV exposure and damage and as such are not useful early indicators that could be used as warning signs. There is an unmet need to identify skin damage as well as the presence of cancer with an early indicator, which could lead to more effective treatments.

We have identified Syk (spleen tyrosine kinase) as an important biomarker of skin photodamage. Our cellular data in human dermal fibroblasts (HDFs) indicate that Syk enhances MMP-1 expression upon UV exposure, while both a Syk inhibitor and Syk siRNA were able to inhibit MMP-1 expression. Our in vivo experiments confirmed a positive correlation between Syk and collagenase (MMP-13) in the skin of hairless mice. We have also identified elevated Syk expression in biopsy samples from the skin of patients exposed to UV compared to unexposed skin. An examination of squamous cell carcinoma (SCC) samples and basal cell carcinoma (BCC) has suggested increased Syk expression in tumor tissue.

For diagnostic purposes we developed suitable staining and detection methods. Sections from Mohs micro-surgeries can be used to microscopically evaluate tumor lesions and to guide the further removal of tissues using a fluorescent marker and Syk antibody. For in-vivo application, it is required to efficiently detect the marker in deeper skin layers and to avoid interference with skin auto-fluorescence. For that purpose we encapsulate the fluorescent marker into liposomes. Once the liposomes diffuse into the skin, they burst, releasing the conjugated dye-antibody complexes, and allowing them to bind to Syk. We are using a hyperspectral imaging system to detect spectral profiles allowing us to differentiate tissue auto-fluorescense from the specific signal of the biomarker.

Funding: This study is funded by the Coulter Translational partnership program, Coulter Foundation