

SYK - A New Biomarker for Early Skin Cancer Detection and Localization

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Early skin cancer diagnosis - an unmet need

There is no established molecular indicator of the level of skin UV damage, and its correlation to the onset of skin cancers. Matrix metalloproteinases (MMPs) are well known indicators of skin damage, but these changes are detected only after considerable damage has been done to skin.

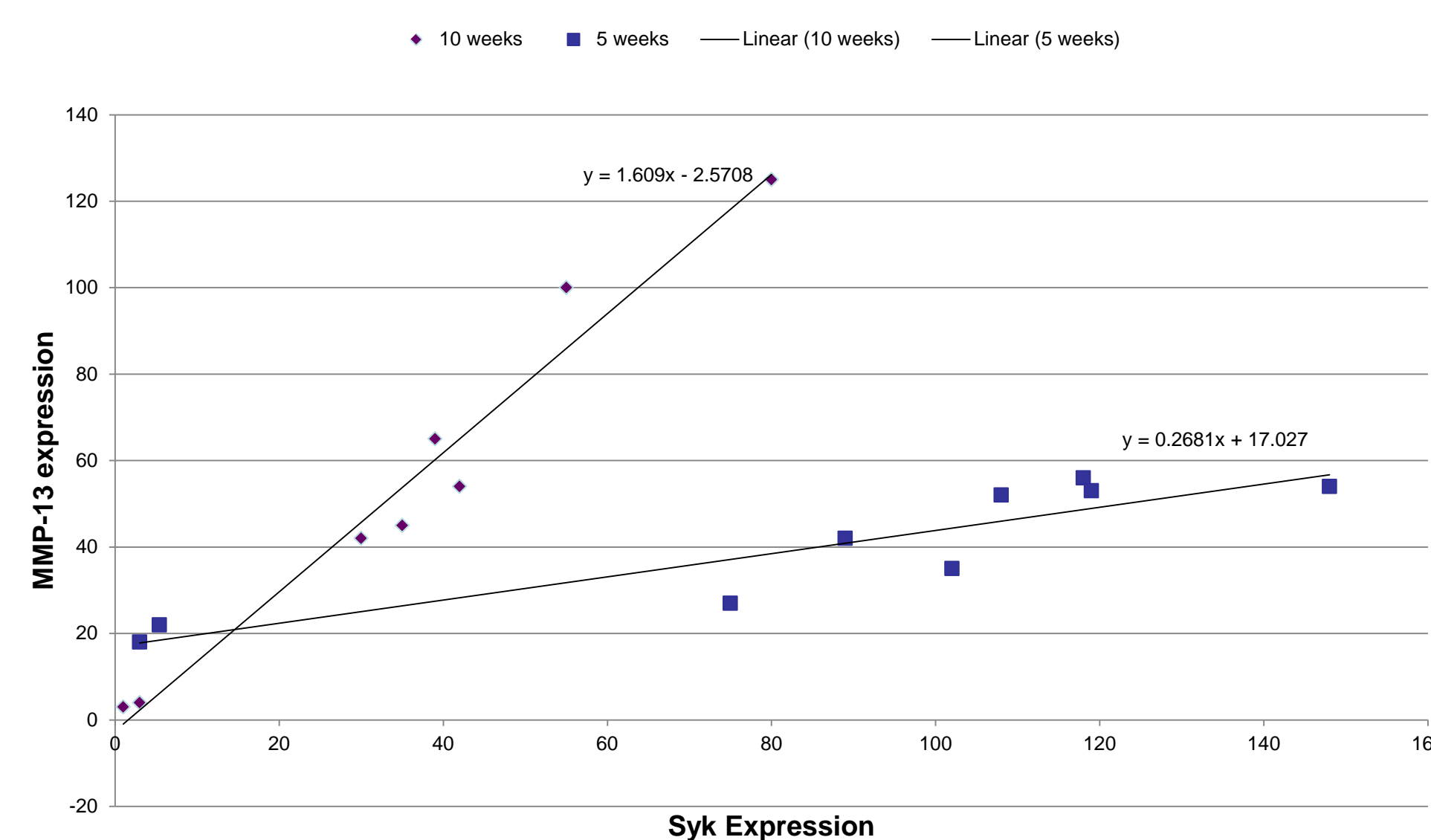
There is an unmet need to early diagnose skin damage and presence of cancer lesions and provide a better indication of the exact localization of lesions, which could lead to more effective treatments.

We have indentified a new biomarker to diagnose skin cancer. Spleen tyrosine kinase (Syk) is upstream of matrix metalloproteinases in the signal transduction pathway. There is a significantly higher expression of spleen tyrosine kinase in different skin cancer types as compared to control tissue.

Skin Cancer Types

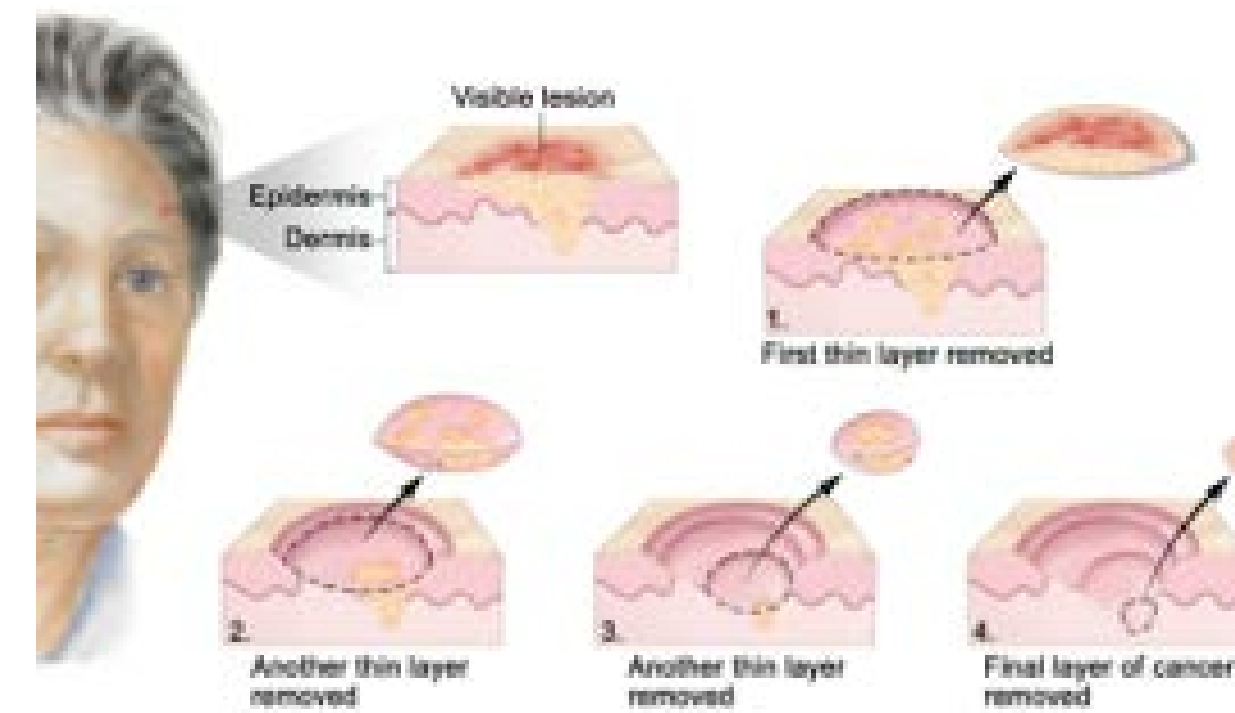
- Skin Cancers make 50% of all cancers, 1 million new cases/year
- Basal Cell Carcinomas (BCC) – 80% of new skin cancers
- Squamous Cell Carcinomas (SCC) – 16% of new cases
- Melanomas – 4%, but most deadly

Early Detection



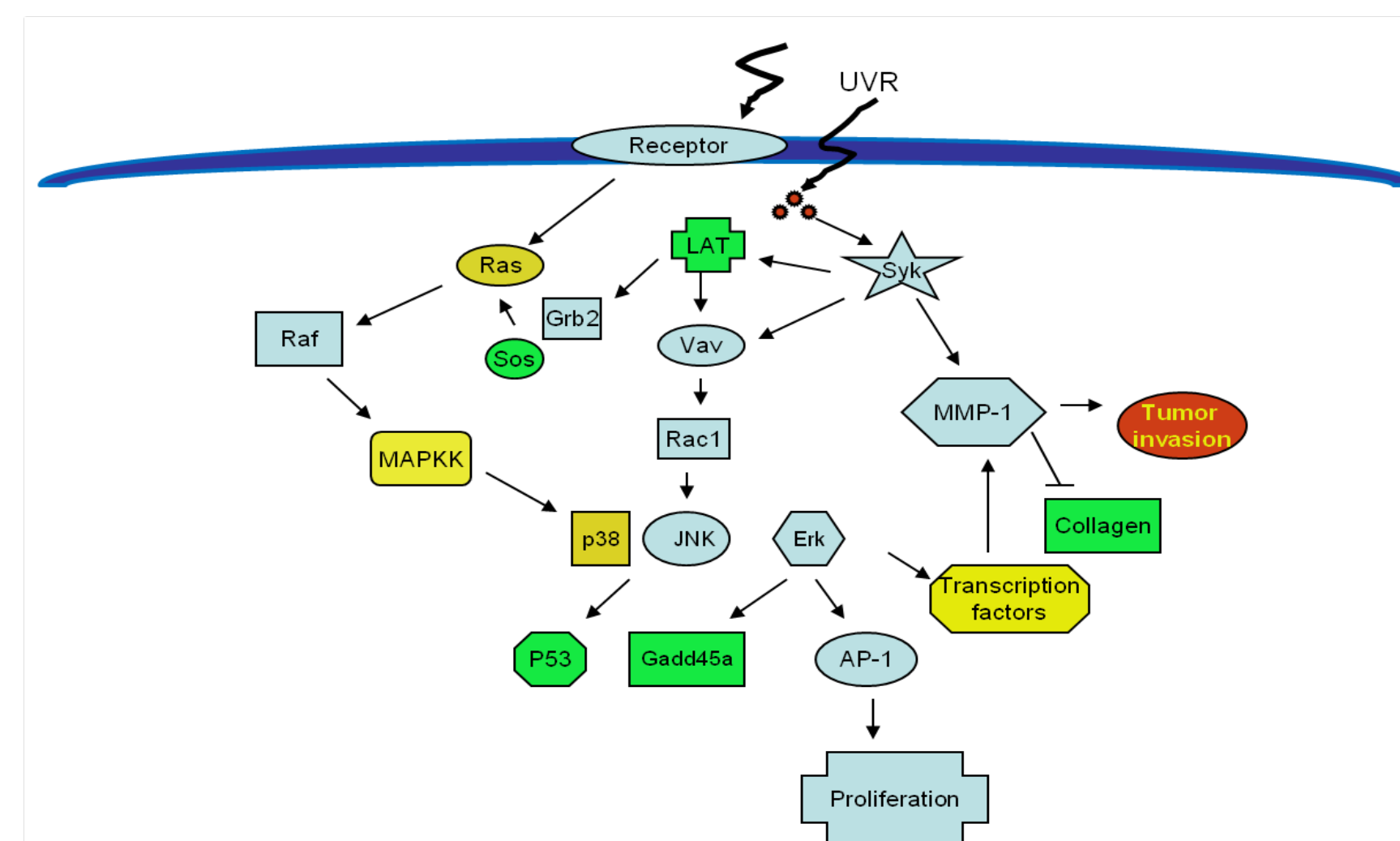
We found Syk to be increased at the end of week 5 after UV radiation, whereas MMPs do not show a significant increase until week 10. For these experiments we developed and applied a solar radiator in a mouse model.

Improved Localization: Mohs Surgery



During Mohs micrographic surgery the tumor margins are identified by transformed cells and this highly subjective method can lead to incomplete tissue removal and recurrence. Using Syk as a biomarker can help to better delineate cancerous tissue.

Deciphering Molecular Mechanisms



UV radiation activates Syk, which is upstream of a signaling cascade including the tumor marker MMP-1.

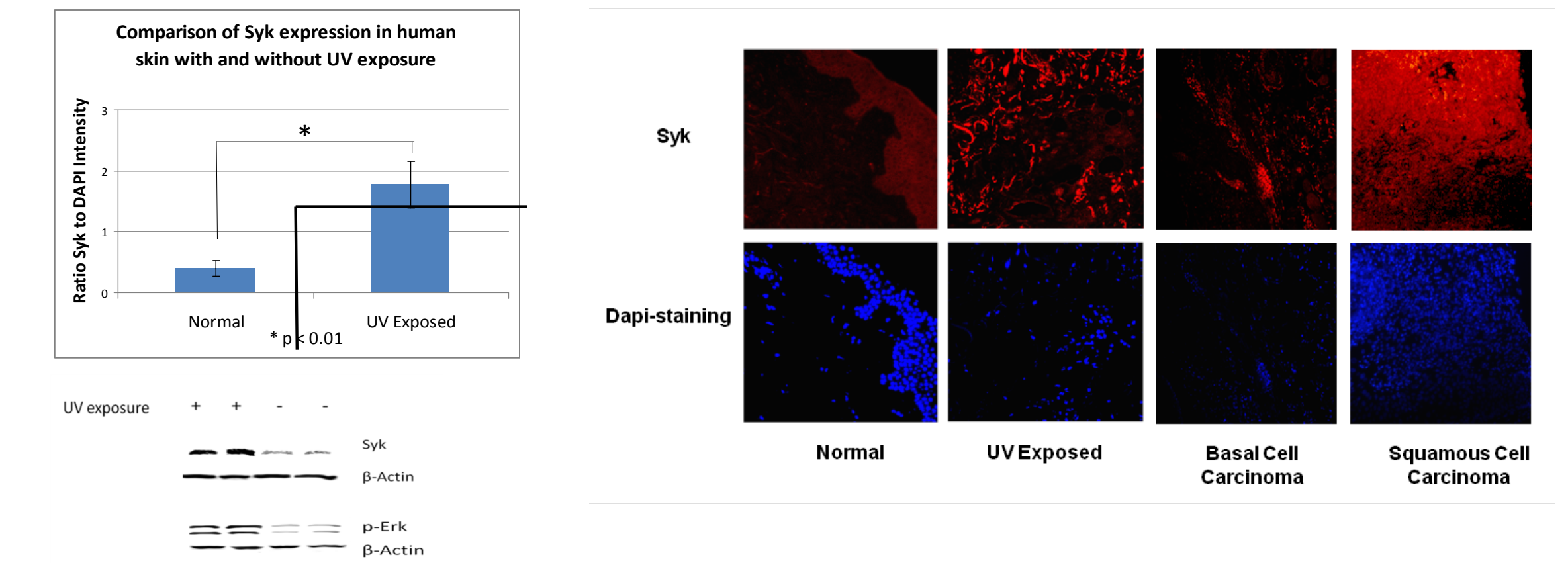
Project Milestones and Goals

- UV exposure increases Syk expression in vitro as well as in vivo.
- Changes in Syk precedes MMP-1 expression, it can serve as an early marker for cancer lesions.
- Syk is overexpressed in skin cancers including SCC, BCC and Melanoma, compared to normal skin.
- To establish a device and procedure to use Syk as a diagnostic marker in vivo.
- To investigate the merit of spleen tyrosine kinase as a means of delaying progression or curing skin cancers.

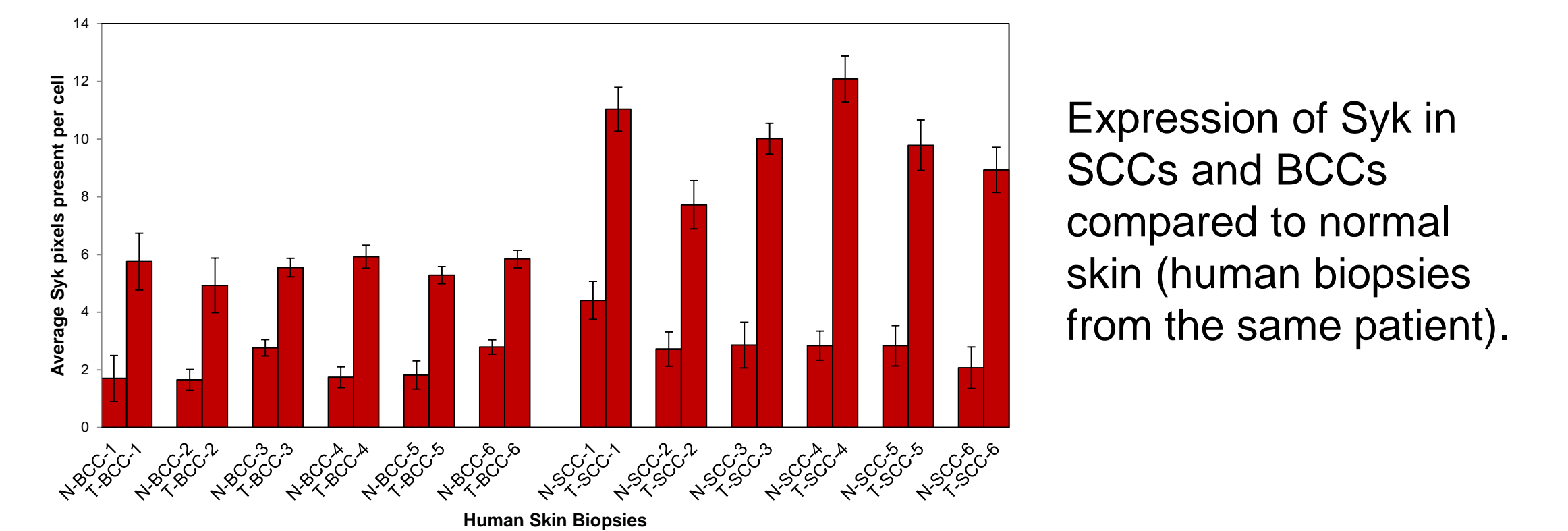
Acknowledgements

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UV Exposure, SCC and BCC cancer

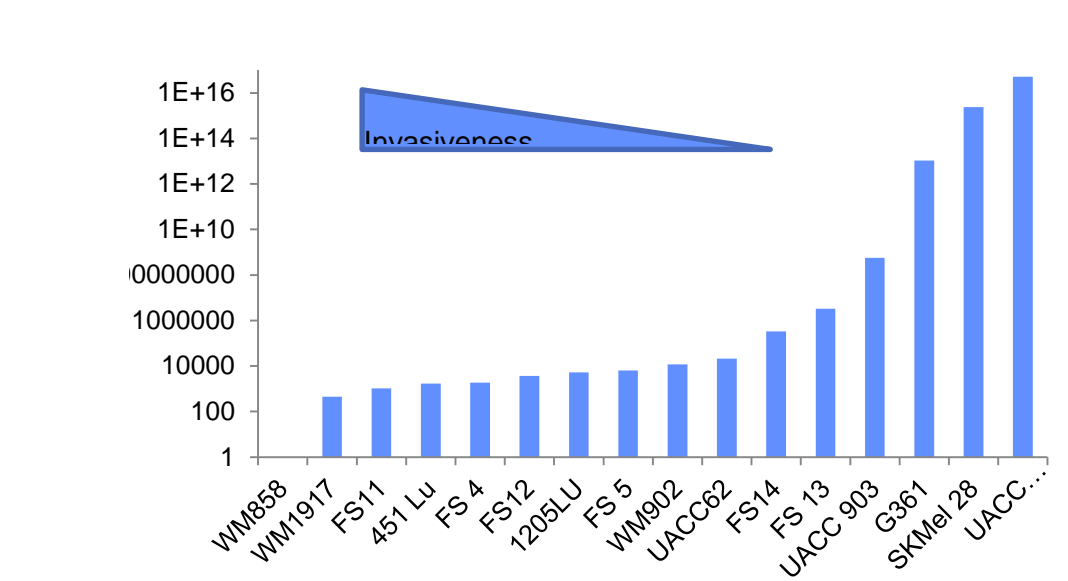


Syk is overexpressed in UV exposed skin. Chronic sub-erythemal UV doses on SKH1 hairless albino mice showed a significant increase in the expression of Syk. Immunofluorescence on various tissues showed the extent to which spleen tyrosine kinase is expressed in them.

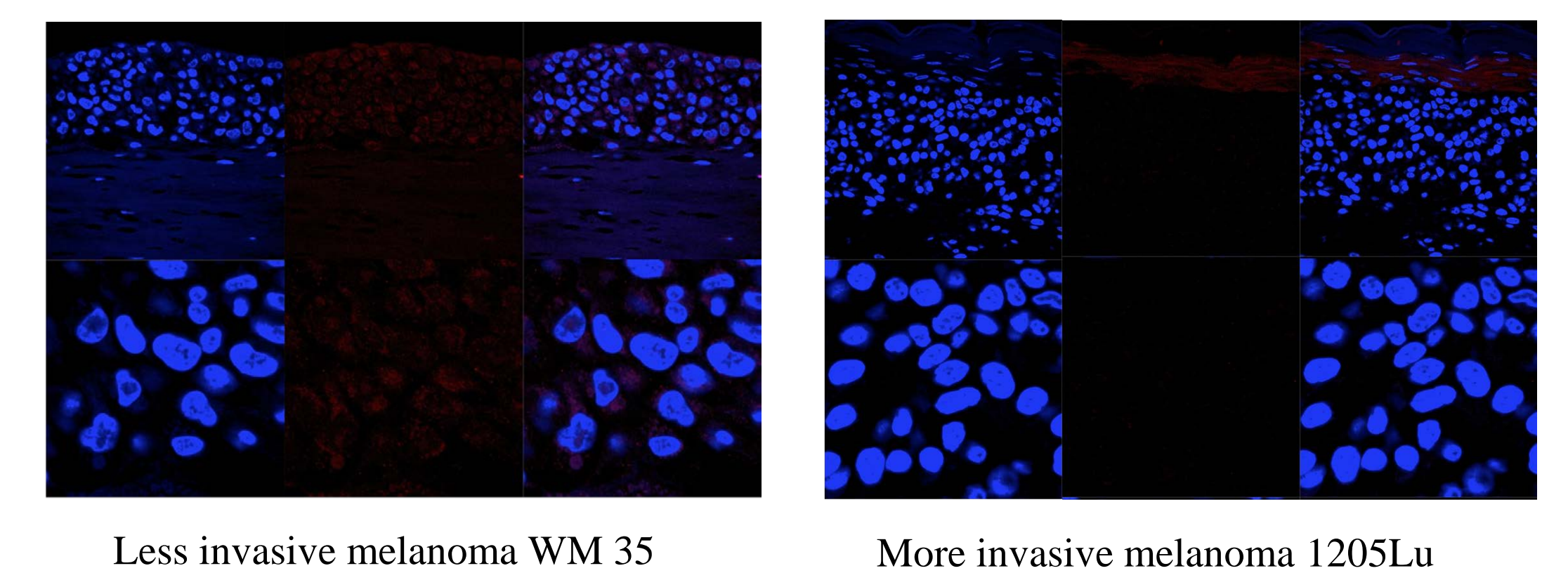


Expression of Syk in SCCs and BCCs compared to normal skin (human biopsies from the same patient).

Future Work: Role of Syk in Melanomas



PCR performed on melanoma cell lines that Syk correlates to the invasiveness on the cell line. More invasive the cell line, less expression of Syk.



Less invasive melanoma WM 35 More invasive melanoma 1205Lu

Affiliations

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