Skin aging is the result of intrinsic aging and photoaging, due to UV exposure, that both share important molecular features including alterations of proteins. The aim of this work is to better understand the role of glyoxalases in the protection of proteins and in the detoxification of glyoxal (GO) and methylglyoxal (MG) during skin aging. Analyses of skin sections from young and old donors photoexposed vs photoprotected show that Glyoxalase 1 (Glo1) localizes exclusively in the epidermis basal layer. Surprisingly, its expression is increased in aged skins and is accompanied by a decrease of carboxymethyllysine modified proteins in this skin compartment. We have also shown that Nrf2, which regulates the expression of Glo1, declines in aged epidermis, suggesting that Glo1 is regulated by a different pathway in the epidermis progenitors.

To understand the role of glyoxalases in response to dicarbonyl stress in keratinocytes, HaCaT cells were subjected to a 24h GO or MG stress. A significant increase of glycated proteins was observed immediately after stress, together with a decreased activity of Glo1 with no change of its expression. Recovery leads to the reactivation of the enzyme.

Moreover, cellular clones overexpressing Glo2 or inhibiting for Glo1 have been shown to exhibit less or more glycated proteins respectively. They will be used to identify preferential protein targets of glycation in skin cells by proteomic studies.