The work presented in this thesis is related to the initiation of UV-induced immunosuppression in the skin. This phenomenon is induced by sunburn radiation (UV-B) and it can cause recrudescence of skin infections or skin cancer in the long term. The sunburn radiation is absorbed by many different biomolecules present in the upper skin (epidermis). One of the main epidermal UV-absorbers is trans-urocanic acid (trans-UCA) and this UCA-isomer can be photoisomerized by UV-radiation into cis-UCA. Cis-UCA has been considered for almost two decades as one of the main inducers of UV-induced immunosuppression.

In Part I our results show that cis-UCA is a rather persistent compound in the human epidermis. Due to the persistent presence of this putative immunosuppressant, the following question can be asked: do we live in a state of continuous immunosuppression? This view does not make much sense, unless there would be a threshold level to exert a cell triggering effect or cells may be adapted to substantial cis-UCA levels. In the course of UCA research through the 80s and 90s it became clear, however, that cis-UCA did not mimic every effect of UV on immunity and its working mechanism is still not clarified. This discrepancy had led us to speculate that UCA can be converted by UV-exposure into oxidized derivatives that are jointly responsible with cis-UCA for the observed immunosuppression.

In Part II it was shown that both trans-UCA and cis-UCA are good hydroxyl radical scavengers and that both UCA isomers can be converted into several photooxidation products. Some of these products have been identified, among them are three imidazoles. Moreover, the presence of these imidazoles was also demonstrated in UV-B exposed corneal layer of the human skin. It was shown here that the UCA oxidation products are only formed by sunburn radiation (UV-B) and not by UV radiation that can pass window glass (UV-A). Cis-UCA, on the other hand, is formed by UV-B and UV-A from trans-UCA.
In Part III the immunobiological activity of cis-UCA, as well as that of the UCA photooxidation products, were tested for their systemic response in a murine model of contact hypersensitivity (CHS). The systemic suppressive effect of three imidazoles on CHS response was at least as strong as that observed with cis-UCA when tested in combined form and when having lower concentration than cis-UCA.

The above results indicate a role for UCA (photo)oxidation products in UV-B-induced systemic immunosuppression and these new aspects are fully outlined in this thesis.