

Chronic inflammation is considered to be one of the hallmarks of carcinogenesis, as it promotes tumor formation and progression. It is well known that inflammation can stimulate carcinogenesis by "supplying" to tumor microenvironment the relevant micromolecules, such as growth factors, antiapoptotic and proangiogenic factors, as well as enzymes that modify the extracellular matrix. The mechanisms controlling the activation of inflammation are still unexplored. However, recent findings indicated that key role in the initiation of inflammation could be played by large cytoplasmic protein complexes which core consists of nucleotide-binding oligomerization domains (NOD), known as inflammasomes. Although many NOD-like receptors may form inflammasomes, two of them have been well described: NLRP1 (NOD-Like Receptor Family Pyrin Domain Containing 1) and NLRP3 (NOD-Like Receptor Family Pyrin Domain Containing 3). In general, the action of NLRP1 and NLRP3 is to transform the procytokines IL-1 $\beta$  and IL-18 into active forms that stimulate the inflammatory process by inducing a number of other proteins (i.e., IL-6, TNF, IL-17).

Although the activation of NLRP1 / NLRP3 inflammasomes may be dependent on many endo- and exogenous factors, from the perspective of our long-term research, ultraviolet radiation (UVR) seems to be the most interesting regulator of their function. This is important because UV radiation is also a major risk factor for the development of non-melanoma skin cancers. It is therefore highly probable that there is a causal relationship between the activation of inflammasomes and the process of skin carcinogenesis, which despite many studies, did not have an accurate description. Therefore, the main goal of the study is to determine the role of NLRP1 and NLRP3 inflammasomes in the pathogenesis of non-melanoma skin cancers. This will be the first study that will precisely assess the disturbance of expression of these protein complexes in NMSC, including the tumor location. What is more, thanks to the use of appropriate lamps emitting a diverse spectrum of UVR, we will follow the activation of these two protein complexes under the influence of different doses of this radiation. The research is innovative not only due to the rich methodology used, but most of all a multidirectional approach to the subject which so far has been studied poorly.

The works on the effects of ultraviolet radiation on the process of skin carcinogenesis has been conducted by Principal Investigator and his team for several years, which is why we have appropriate experience both in cell culture and the use of molecular biology techniques appropriate for this purpose.