Cystatins comprise a large superfamily of related proteins with diverse biological activities. They were initially characterised as inhibitors of lysosomal cysteine proteases, however, in recent years some alternative functions for cystatins have been proposed. Cystatins possessing inhibitory function are members of three families, family I (stefins), family II (cystatins) and family III (kininogens). Stefin A is often linked to neoplastic changes in epithelium while another family I cystatin, stefin B is supposed to have a specific role in neurodegenerative diseases. Cystatin C, a typical type II cystatin, is expressed in a variety of human tissues and cells. On the other hand, expression of other type II cystatins is more specific. Cystatin F is an endo/lysosome targeted protease inhibitor, selectively expressed in immune cells, suggesting its role in processes related to immune response. Our recent work points on its role in regulation of dendritic cell maturation and in natural killer cells functional inactivation that may enhance tumor survival. Cystatin E/M expression is mainly restricted to the epithelia of the skin which emphasizes its prominent role in cutaneous biology. Here, we review the current knowledge on type I (stefins A and B) and type II cystatins (cystatins C, F and E/M) in pathologies, with particular emphasis on their suppressive vs. promotional function in the tumorigenesis and metastasis. We proposed that an imbalance between cathepsins and cystatins may attenuate immune cell functions and facilitate tumor cell invasion.

Key Word:
cystatin; stefin; cathepsin; inhibitor; protease; proteolytic activity; immune cells; tumor; disease