

Cancer patients suffer from chronic impairment of natural defense mechanisms commonly referred to as immunosuppression. Defective immunity increases the risk of infectious (mainly bacterial) complications and contributes to increased mortality. Defective immunity is caused by many factors that include cancer-related dysregulation of the immune response, adverse effects of chemo- and radiotherapy on the immune system, as well as chronic diseases coexisting in cancer patients. Recent studies indicate that in advanced cancer there is a massive expansion of erythroid progenitor cells (EPCs) that seem to be a major population of cells inhibiting multiple mechanisms of the immune system. However, elimination of EPCs is not feasible as these cells are direct precursors of erythrocytes (red blood cells) and are necessary for the well-being of the organism. Our preliminary studies revealed that EPCs use a specific enzyme that seems to be responsible for the majority of their immunosuppressive properties. Thus, the major goal of our studies is to investigate whether targeting this enzyme will ameliorate EPCs-associated immune dysregulation and might be used to increase the resistance to infections with the most typical bacteria that are being the cause of premature death of cancer patients. The studies will be carried out in animal model of plasma cell myeloma (PCM). This is a tumor originating from the terminally differentiated B cells. It develops mainly in elderly patients and leads to compromised immune system, and end-organ damage typically encompassing renal failure, anemia, or bone lesions. Despite a significant improvements in the available treatment modalities that became available over the recent years, PCM still remains a largely incurable disease, with a median survival of up to 6 years. Moreover, with the ageing society, the incidence of this disease is constantly growing. The results of this project might be helpful in elucidating molecular mechanisms of immune dysregulation and in identifying novel targets for the management of cancer patients.