MOI Project 14

Role of the chemokines CCL17 and CCL22 during infections with *Salmonella* Typhimurium and metabolic stress

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The chemokines CCL17 and CCL22 are mainly secreted by antigen presenting cells and regulate the recruitment of T cells and other immune cells. They signal via the receptor CCR4 which is expressed on a variety of immune cells, including T cells, basophils, mast cells, macrophages and dendritic cells (DCs). Although both ligands interact with the same receptor, CCL17 exerts a more immunostimulatory role in allergies or inflammatory diseases, whereas CCL22 is associated with immunosuppressive functions in the tumor environment. This might be caused by different binding properties of the chemokines to CCR4, thereby inducing different signaling pathways or efficacies, a phenomenon called biased agonism. The function of CCL17 and CCL22 in infectious diseases is not well understood, yet. Here, we want to analyze the role of CCL17 and CCL22 after chronic infection of mice with an attenuated *Salmonella* Typhimurium (STM) strain, which allows not only to focus on early host defense functions but also to analyze adaptive immune responses. We could already show that CCL17 and CCL22 are upregulated after acute infection with STM in mouse models, but their interference with T cell responses during chronic infections is so far unclear. Therefore we want to elucidate the contribution of the chemokines CCL17 and CCL22 in the induction of T cell responses in chronic infection with STM. Obesity is one of the biggest health problems worldwide and increases the likelihood of type II diabetes or cardiovascular disease, but is also a risk factor for infections. Obesity causes a weak, chronic inflammatory response which does not only alter metabolic responses but also influences immune responses. These changes affect adipose tissue, but also other organs such as lung and intestine and can enhance the susceptibility for infections. We found that naive CCL17- and CCL22- double deficient female mice possess a higher body weight than wild-type animals. Since we were also able to detect the expression of CCL17 in adipose tissue, it is possible that CCL17 and CCL22 play a previously unknown role in the homeostasis and/or differentiation of adipose tissue. Therefore, we want to characterize the function of the chemokines after chronic infection with STM, as well as in metabolic syndrome after high-fat diet and elucidate the host defense response to STM infection in animals with metabolic syndrome.