Impacts of uremia on the shaping of systemic and local innate immune responses

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Abstract

During single- or multiple- species infections individuals run increased risk for tolerance break, auto-inflammatory disorders and solid organs as well as tissues chronic inflammation. Some published epidemiologic data support an association between various infections and chronic kidney disease (CKD). Furthermore there are pieces of evidence for effects of CKD on condition of skin, pulmonary-, oral- or other soft tissues and increased levels of infections were observed in hemodialysis patients with severe CKD.

In this experimental approach we will conduct investigations aimed to **determine the systemic consequences of CKD**. We assume that chronic kidney disease which is associated with accumulation of uremic toxins affects systemic inflammation and modulate the systemic responses of immune system. Because several studies focus already on CKD and systemic adaptive immunity, we will dedicate our special interest to **innate immune-regulatory molecules** and **immune-regulatory microRNAs.** Examination of such regulatory mechanisms of defense and homeostasis is necessary to fully understand the effect of uremia on pathogen overgrowth. The exact mechanism by which **CKD enhance the susceptibility to infections** is yet not well understood. We hypothesized that **uremia induces so called `immune tolerance`** and that tissues are more **prone to colonization with pathogen species upon uremic conditions** (analogous to immunosuppressive conditions observed after septic shock). As consequence it is possible that the progression of infection and its nature will significantly differ from the one induced during non-uremic conditions. Furthermore the effects of **the inflammatory processes associated with local infections on further progression of chronic kidney disease** will be assessed. Number and nature of specific receptor components on epithelial cells and resident and systemic immune cells may correlate with incidences of symptomatic infections and renal scar formation and the level of uremic toxins. Such findings could change the present perception on treatment of infections during renal impairment.