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Complexity of immune suppression underlying immune privileges in stem system

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Motivation and Aim: An ability to evade immune surveillance is called immune privileges. Immune privileges are recognized as a major issue and are wildly studied in context of cancer and cancer stem cells. Despite a lot less attention, there are studies demonstrated the immune privileges of non-pathologic stem cells in different tissues. We managed to demonstrate immune privileges of mesenchymal stem cells [1]. In the following review, I marked a deep mutual interference between immune and stem cells, and basing on the complexity of stem cells regulation suggested the term “stem system” [2]. Yet, the question about mechanisms underlying the phenomenon stayed unconsidered. I further continued to study literature for described molecular mechanisms responsible for immune suppression.
Methods and Algorithms: While the aim of the study is to aggregate data for non-pathologic cells and tissues, a significant part of data arises from studies of cancer or other pathologies. There are certain changes in pathologic regulation, it allows to identify associated molecular mechanisms. At the same time, there are mechanisms utilized by pathology, but not broken by itself. We can take examples from cancer, where tumor cells reprogram non-tumor endothelial or immune cells to support and protect tumor microenvironment.
Results: In addition to several mechanisms demonstrated to be involved in non-pathologic stem cells immune privileges, there are other mechanisms demonstrating contribution to immune suppression for pathologic conditions and for normal one. In general, immune suppression is activated by activation of immune cells to provide proper control and to prevent excessive damage. Immune suppression is performed by specialized immune cells and by other cells in various tissues, including stem cells. Many mechanisms are common for different cells, but could be differently regulated by side factors. Depending on the conditions, a signal can activate or suppress an immune cell. Conditions could be presented by a switching molecule or by quantitative values, as pH. Components of signal pathways are controlled by transcription, splicing and post transcription modifications. Variations in abundance of soluble and membrane bound signaling molecules can provide nonlinear response. Some receptor ligand relations still don’t identified. There are reports of new mechanisms involving microvesicles and contained in them long non-coding RNA and micro RNA. Important notice is that mechanisms are tangled with each other and other regulations. Partial duplications of studied mechanisms are common to provide robust control over immunity.
Conclusion: There are various immune suppressing mechanisms contributing to the complex network and to the formation of immune privileges. Mechanisms of immune suppression are required for the immune system to contribute to regeneration and to support homeostasis of stem cells. The stem system is also integrated in immune

regulation and may suppress the immune system. There are plenty of studies demonstrating individual mechanisms or their combination. The amount of available information makes aggregation a complex task requiring new automated approaches. The problem expands beyond a quantity of information to its complexity. As immune system is a protector from foreign invasions, restricting mechanisms could not afford to be simple. If an immune suppression would be achieved by simple regulation, it could be used by invading pathogens and so evolutionary discarded. On the contrary, immune suppressing mechanisms should be enigmatic as well as robust to protect and to support homeostasis. Deciphering immune regulation can provide solutions for medicine. Particular studies consider a number of factors, but there are always more unstudied factors to be involved. The cost of experimentally testing factor by factor grow faster than exponentially with the number of factors. It is worsened by differences between human and model animal. This results in the lack of knowledge forming a natural barrier to model on the aggregated data.

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