Development of innate immune cells from human pluripotent stem cells.

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Public Summary:
Pluripotent stem cells (PSCs) are cells that have the potential to self-renew by dividing and can give rise to all cells of the adult body. Both embryonic stem cells and induced pluripotent stem cells (cells that are reprogrammed from adult tissues) are pluripotent. Mouse and human PSCs have been widely used to study the development of blood cells and cells of the immune system. Although not all cells can be derived with the same efficiency, immune cells such as natural killer (NK) cells and macrophages can be easily produced from PSCs and enable development of new cell-based therapies. NK cells and macrophages are part of the innate immune system, the first line of defense against malignancies and infectious disease. Human embryonic stem cell (hESC)- and induced pluripotent stem cell (iPSC)-derived NK cells can be produced in large quantities suitable for translation into clinical trials. Additionally, PSCs can be genetically modified to produce hESC/iPSC-derived human NK cells with enhanced antitumor activity. These engineered NK cells can express a stabilized version of the high-affinity Fc receptor CD16, chimeric antigen receptors, or other strategies to enable more potent and targeted cellular immunotherapies. Moreover, macrophages can also be routinely and efficiently produced from hESCs and iPSCs as a tool to expand our knowledge of the basic biology of these cells. hESC- and iPSC-derived macrophages can also be employed as a novel approach for cancer immunotherapy, as well as a strategy to repair or regenerate diseased and damaged tissues and organs.

Scientific Abstract:
Mouse and human pluripotent stem cells have been widely used to study the development of the hematopoietic and immune systems. Although not all cells can be derived with the same efficiency, immune cells such as natural killer (NK) cells and macrophages can be easily produced from PSCs to enable development of new cell-based therapies. NK cells and macrophages are part of the innate immune system, the first line of defense against malignancies and infectious disease. Human embryonic stem cell (hESC)- and induced pluripotent stem cell (iPSC)-derived NK cells can be produced at a clinical scale suitable for translation into clinical trials. Additionally, PSCs can be genetically modified to produce hESC/iPSC-derived human NK cells with enhanced antitumor activity. These engineered NK cells can express a stabilized version of the high-affinity Fc receptor CD16, chimeric antigen receptors, or other strategies to enable more potent and targeted cellular immunotherapies. Moreover, macrophages can also be routinely and efficiently produced from hESCs and iPSCs as a tool to expand our knowledge of the basic biology of these cells. hESC- and iPSC-derived macrophages can also be employed as a novel approach for cancer immunotherapy, as well as a strategy to repair or regenerate diseased and damaged tissues and organs.