ImmunoTools *special* Award 2018

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Application of hiPSC-derived macrophages for disease modelling

Macrophages are specialised cells present throughout the body in almost all tissues and exhibit diverse roles depends on the local environment. Macrophages not only provide protection by clearing up invading pathogens, but also play a key role in homeostasis, angiogenesis and tissue regeneration by the secretion of wide range of cytokines, chemokines and growth factors. Functional abnormalities of macrophages underlies various disease pathogenesis, including but not limited to Tuberculosis (TB), Hereditary diffuse leukoencephalopathy with axonal spheroids (HDLS), HIV infection, cardiovascular diseases and cancer. The process of macrophage activation depending on external stimuli, on the other hands called as polarisation gives rise to different subsets of macrophages such as M1, M2a, M2b, M2c and M2d. Establishing an *in vitro* disease modelling using human macrophages would great facilitate to understand underlying disease pathologies in various diseases which will ultimately help us in screening of candidate drugs. However, peripheral blood-derived macrophages or transformed cell lines remain the major sources at the moment. Both have limitations, as getting peripheral blood is invasive and dependent on the donor availability and one has to consider batch to batch variation due to the differences among donors. Whereas, transformed cell lines are often different from primary macrophages.

Human induced pluripotent stem cells (hiPSCs), have the ability to self-renew and differentiate into diverse cell types of the body, including macrophages. Thus, hiPSCs offer a great source of unlimited number of patient-specific monocytes and macrophages. Especially, because patient-specific macrophages are often difficult to obtain, as well as secure as a renewable source of the cells from the same donor. However, scientists/researchers has to take many aspects into account before considering hiPSC-derived macrophages as model systems to study primary macrophages.

Recently, we developed an efficient protocol to differentiate human macrophages from hiPSCs using serum and feeder-free conditions in relatively short period of time (unpublished data). Based on preliminary experiments we observed that hiPSC-derived macrophages had similar morphology and gene expression profiling compared to human primary macrophages.

However, we want to further extend this analysis and check their ability to produce cytokines and chemokines based on various stimuli. Also, we want to investigate their functionality especially, in terms of phagocytosis and inflammation. Furthermore, we want to do a side-by-side comparison of hiPSC-derived macrophages with primary macrophages in order to identify similarities and differences between these two sources, in terms of surface markers expression, cytokines production and functional capabilities. These results could provide researchers a great scope to choose a suitable platform for disease modelling and drug screening studies using hiPSC-derived macrophages as an alternate source to primary macrophages. In order to perform a thorough comparison between hiPSC-derived macrophages and primary macrophages, we need a large panel of macrophage-related antibodies for flow cytometry and cytokine panels. The reagents from ImmunoTools can help us greatly in our study with hiPSC-derived macrophages and lay a firm foundation for their later application in disease modelling and drug development.

To conclude, studying macrophage biology has utmost importance to the society, as by understanding their role in highly prevalence diseases such as cardiovascular diseases and cancer, can help us in identifying potential therapeutic drugs to prevent or cure these diseases.

ImmunoTools *special* AWARD for **Xu Cao** includes 25 reagents

FITC - conjugated anti-human CD3, CD11c, CD47, CD86

PE - conjugated anti-human CD4, CD11a, CD36, Annexin-V

human ELISA-set (for one 96 plate): human IL-10, human IP-10/CXCL10,
human MCP-2/CCL-8, human TNF-alpha

recombinant human cytokines: rh G-CSF

DETAILS more AWARDS