Simposio Internacional: Biointeractómica

***International Symposium**: Biointeractomics*

Sevilla, 30 y 31 de octubre de 2012
Sevilla, October 30-31, 2012

Towards an understanding of immune cell sociology based on single-cell analysis

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Mammalian immune system is a highly dynamic and complex system. In the immune system, cell-cell interactions are mediated by physical contact and humoral factor. In particular, the long-range cell-cell interactions by humoral factors (*i.e.*, cytokines and chemokines) play a crucial role in homeostasis of the immune system as a whole. To get a sociological viewpoint of the immune homeostasis, we have applied several different methods to monitor production/secretion of humoral factor(s) from immune cells at the single-cell level as well as at the cell ensemble level. Because we are most interested in the responses of macrophage and/or monocytes after stimulation of endotoxins such as lipopolysaccharide (LPS), we tried to monitor the changes in cytokine/chemokine production in population along the time. The data indicated that the cytokine production levels, either at the mRNA level or at the secretion level, varied widely from cell to cell even when we used a genetically cloned cell line of macrophage-like cells. Heterogeneous responses to LPS in cell population were also observed in human monocytes isolated from healthy donors. For measuring the secretion of cytokine/chemokine from a single cell in a time-resolved manner, we developed a new method which enables us to simultaneously monitor cytokine/chemokine secretion and intracellular events by fluorescence microscopy. On the basis of the datasets thus obtained at the single-cell level, it now becomes possible to start to discuss how the immune homeostasis is robustly achieved under a sophisticated regulation of cell-cell interactions at the systems level.