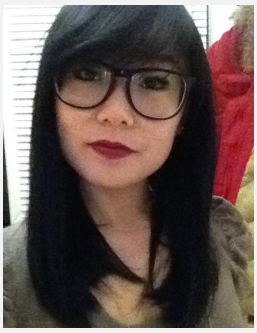
ImmunoTools *special* Award 2016



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The role of ADAR1 in myeloid differentiation

RNA editing is a post-transcriptional mechanism able to increase the variability of the RNA molecules and to create new protein isoforms from a single gene (1). The most frequent type of RNA editing in mammals is the chemical conversion of adenosine (A) to inosine (I) in double-stranded RNA (dsRNA).

Inosine is interpreted by the apparatus of splicing and translation of the cell as a guanosine thus introducing a mutation in a variable percentage of the molecules (2). Those mutations can modify both RNA primary sequence (such as codons, splicing sites and miRNA seed sequences) and structures (for example pre-miRNAs) with different effects on the RNAs and edited protein they produce. Several editing events in the coding regions have pivotal physiological roles and affect protein sequence (recoding events) or function (3). The RNA editing is catalyzed by three enzymes called ADAR (Adenosine deaminase acting on dsRNA): ADAR1 and ADAR2 are ubiquitously expressed and catalytically active, whereas ADAR3 is expressed exclusively in the brain and it is inactive in *in vitro* assays.

Recent studies have identified a correlation between RNA editing and the development of the hematopoietic system. These studies have indicated how the action of the ADARs is essential for hematopoietic stem cells (HSCs) self-renewal (4), for embryonic development, as demonstrated in knock-out mice. Moreover ADAR1 has been shown to promote malignant progenitor reprogramming in chronic myeloid leukemia. However, the understanding of the role of ADAR1 in the differentiation of hematopoietic system is still at the beginning (5).

During my master work, I contributed to analyze the expression and activity of ADAR1 in the maturation of macrophages derived from two monocytic cell lines differentiated *in vitro* with different reagents (PMA, GM-CSF+VitD3). Now we have generated stably ADAR1-silenced U937 cell clones to study how ADAR1-mediated editing activity contributes to differentiation and cell growth.

To this aim silenced U-937 cells will undergo differentiation by different stimuli such as PMA or GM-CSF/VitD3 and the editing activity will be correlated to cell cycle progression and differentiation. The latter will be monitored by specific MoAbs against surface markers such as CD11b, CD14, CD71, CD163, CD54, CD16, CD32, HLA-ABC, HLA-DP, HLA-DR, CD1a as well as for the intracellular expression of specific markers.

References:

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