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Dendritic cells molecular signatures as a tool for adjuvants selection

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Activation of cells of the innate immunity such as macrophages and dendritic cells (DCs) is critical to mount effective adaptive immune responses. A new approach to enhancing the efficacy of vaccine adjuvant is to enhance DCs maturation and activation. This property can be exploited to develop specific cell-based assays for adjuvant selection. Research in our lab is focused towards the development of novel DCs based assays that can be used to identify and to improve adjuvant and immuno-modulator formulations. Using a functional genomics approach we have been able to select a genetic signature of activation of mouse DC in vitro. We used DCs transcriptomes (115 samples) obtained activating the cells with live bacteria and with TLR agonists (LPS, Zymosan, CpG, PolyI:C, PAM3Cys) to derive cell-specific molecular assays. We selected lists composed of 44 and 10 genes able to discriminate between immuno-modulatory and anti-inflammatory molecules in DCs. We validated the signature in vivo in DCs derived from a mouse model of inflammation. The compounds tested were classified with about 90% accuracy. After validation, a novel potential vaccine adjuvant candidate called DiC14-amidine, a cationic liposome, has been tested. The data indicated that DiC14-amidine induces moderate changes in DCs signature as expected for an adjuvant molecule able to avoid excessive immune activation. Therefore, the basic methods to select a genetic signature of DCs activation which may predict in vitro and in vivo activity of a novel adjuvant are presented.

Biography

Maria Foti received her doctoral degree in Biotechnology at the University of Milan in 1996. She did her postdoctoral studies on the molecular mechanisms associated to early events during dendritic cells activation and maturation in the laboratory of Prof. Castagnoli at the CNR, center of molecular and cellular pharmacology, Milan. She is presently assistant professor at the University of Milano-Bicocca and scientific director of Genopolis, a Functional Genomics Consortium at the University of Milano-Bicocca.

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