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Pathway Analysis of Integrin Alpha X/Beta 2 (CD11c/CD18) in the Murine Mononuclear Phagocyte Lineage

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Integrin alpha X (ITGAX, CD11c) is commonly used to discriminate mouse dendritic cells from macrophages. In truth ITGAX expression is more promiscuous than often acknowledged and is expressed in other mononuclear phagocyte (MNP) subsets, for example alveolar macrophages strongly express ITGAX. ITGAX expression has also been observed on lymphocytes and liver natural killer cells. ITGAL (CD11a), ITGAM (CD11b), ITGAX and ITGAD (CD11d) all dimerise with the integrin beta2 subunit (CD18) and act as pattern recognition receptors. As a group these integrins mediate cellular adhesion, phagocytosis and co-stimulatory functions within MNPs; however specific functions following ITGAX binding have yet to be defined. Following the meta-analysis of lineage-specific gene expression signatures in mouse leukocyte populations, the profile of ITGAX mRNA was observed to co-cluster with a restricted set of genes, the products of which suggest novel functions involved in the regulation of the actin cytoskeleton. In order to rationalise the available data and information on ITGAX and its potential functional role, we have attempted to construct a pathway diagram of integrin alpha/beta2-mediated signalling utilising the modified Edinburgh Pathway Notation (mEPN) scheme. In order to achieve this end we have performed extensive mining of the literature guided by protein interaction data available in the STRING (functional protein interaction networks) and REACTOME (a curated knowledgebase of biological pathways) databases. This pathway diagram functions as a detailed and extendable visual aid to understanding the functional context of ITGAX and will be used to generate hypotheses and make in silico predictions of function.