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Detection of the Type I Interferon Response using an IFNβ Reporter Mouse Model

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Type I interferons (IFNs) were initially identified on the basis of their antiviral activities. However, recent studies place these cytokines at the interface between innate and adaptive immunity not restricted to an antiviral response. Structurally, type I IFNs can be grouped into a protein family comprising multiple IFNα subtypes, encoded by at least 13 different genes in the mouse, and a single IFNβ subtype. The canonical pathway for IFNα/β production is initiated by the IRF-3 mediated expression of IFNβ leading to a positive feedback loop via IFN receptor type I and IRF-7. Whereas IFNα/β have been described to be produced by virtually any cell type in response to the appropriate stimulus, tools to track the initial IFNβ producing cells *in vivo* are limited. We therefore generated IFNβ reporter knock-in mice, which express the enhanced yellow fluorescent protein (YFP) from a bicistronic messenger RNA linked by an IRES site to the endogenous IFNβ message. Bone marrow derived dendritic cells (BMDDCs) grown in the presence of Flt3-ligand reported IFNβ production faithfully from the $B220^+$ plasmacytoid subpopulation when stimulated with CpG oligonucleotides in accordance with published data. The amount of IFNβ protein measured by ELISA in the culture supernatants was not significantly altered in BMDDC derived from WT as compared to homozygous reporter mice indicating an undisturbed IFNβ translation from the bicistronic transcript. *In vivo* immunization with the TLR3 ligand poly(I:C) induced YFP expression in a $CD11c^+$ $B220^-$ $CD8^+$ $CD11b^{low}$ DC subpopulations which starts to appear 6h after stimulation in the splenic red pulp, accumulates around the marginal zone by 12h, and subsides again at 24h. Injection of CpG oligonucleotides (TLR9 ligands), however, led to YFP upregulation in plasmacytoid DCs characterized by their $CD11c^{intermediate}$ $B220^+$ $CD8^+$ $CD11b^-$ surface phenotype, which are localized in the splenic white pulp at the T/B cell interface 12h after injection. Further data on *in vivo* viral infection models will be presented.