

Supplemental Table 1: Studies regarding molecules that play a role in eliciting expression of Indoleamine 2,3-dioxygenase (IDO) in Dendritic Cells (DCs).

	DC cell type	Additional information	Reference(s)
“Immunogenic” Agonists			
DC maturation	Human monocyte derived DC	Mature CD83+ DC express IDO	Chung et al., 2009
	Human DCs – DC vaccination	Matured using cocktail of IL-1 β , TNF α , IL-6, and Prostaglandin E2 (PGE2)	Wobser et al., 2007
TNF α	Human monocyte derived DC	As an autocrine secondary signal to elicit IDO after <i>Chlamydia pneumoniae</i> infection in DC	Njau et al., 2009
IFN α	Plasmacytoid DC	Failure to up-regulate IDO after topical PMA-elicited inflammation in IFN α R KO mice	Muller et al., 2008
CpG	Splenic DC	Dose-dependent. Also requires secondary signals.	Baban et al., 2011
IL-32	Human PBMC	Implicated to elicit IDO during HIV infection	Smith et al., 2011
CD40L or LPS	Human CD11c+ DC Human monocyte derived DC	As a second stimulus for heightened IDO production.	Hwu et al., 2000 Favre et al., 2010
CD80/CD86 ligation	Splenic DC (total CD11c+) Splenic DC (total CD11c+)	Failure for T-regs (via CTLA-4) to up-regulate IDO expression in B7-deficient DCs Failure for CTLA-4-Ig to up-regulate IDO expression in B7-deficient DCs	Fallarino et al., 2003 Grohmann et al., 2003b
CD28	Human monocyte derived DC	CD28 expression on malignant plasma cells	Nair et al., 2011
4-1BB	Lymph node CD11c+ DCs	Administration of agonist anti-4-1BB monoclonal antibody <i>in vivo</i> (IFN γ signaling also required)	Choi et al., 2011
IFN γ	Tumor-draining lymph node CD11c+ DC Human monocyte derived DC Plasmacytoid DC	Lack of IDO-up-regulation after immunotherapy in IFN γ -/- mice IFN γ plus 2 nd stimulus resulted in higher expression of IDO Failure to up-regulate IDO after topical PMA-elicited inflammation in IFN γ R KO mice	Harden et al., 2011 Gu et al., 2010 Hwu et al., 2000 Jurgens et al., 2009 Favre et al., 2010 Muller et al., 2008
Signaling Molecules			
Foxo3	Plasmacytoid DCs	Tumor associated DC	Watkins et al., 2011
Acetylated STAT-3	BMDC		Sun et al., 2009
GCN2	Plasmacytoid DC		Muller et al., 2008

Supplemental Table 1: (Continued).

Foxp3	Human monocyte derived DC	Failure to up-regulate IDO after topical PMA-elicited inflammation in GCN2-KO mice Ectopic expression	Lipscomb et al., 2010
AhR	BMDC	Activation by environmental toxin, dioxin (TDCC)	Mezrich et al., 2010 Simones and Shephard, 2011
	BMDC	Activation by an endogenous ligand and tryptophan metabolite, kynurenine	Nguyen et al., 2010
"Tolerogenic" Agonists			
Human chorionic gonadotropin (hCG)	BMDC Human monocyte derived DC	Only after a "first" IDO-eliciting signal (i.e. IFN-gamma)	Wan et al., 2008 Ochiel et al., 2010
PD-1	Splenic CD19+ DC	Lack of IDO induction after CpG if PD-1 interactions blocked <i>in vivo</i>	Baban et al., 2011
CTLA-4	CD8 α - splenic DC	CTLA-4 Ig	Grohmann et al., 2003b
	Splenic B220+ DC and splenic CD8 α + DCs	Both CTLA-4 Ig and endogenous CTLA-4 expressed on T-regs	Mellor et al., 2004
TGF β	Both splenic CD8 α + and CD8 α - DCs	Require secondary cytokine production elicited from DC	Fallarino et al., 2003
	Plasmacytoid DCs	TGF β elicits long-term IDO expression. IDO functions as a signaling protein (independent of enzymatic activity)	Pallotta et al., 2011 Chen, 2011
	Splenic CD8 α + DC	Autocrine TGF β sustains default IDO+ profile	Belladonna et al., 2008, 2009
	Splenic CD8 α -DC	Can switch CD8 α -immunogenic DC to tolerogenic IDO+ DC	

IDO can be elicited by both immune "tolerogenic" agonists, as well as "immunogenic" agonists, as listed. Additionally, intracellular signaling molecules can also play a role in IDO expression in DCs. The IDO agonist is listed along with studies which demonstrated its ability to influence IDO expression in DCs. Additionally, the particular DC subset focused on in the study is noted. Unless indicated as "human", studies utilized murine DCs. BMDC = bone marrow derived dendritic cell.

underlying the sustained nature of IDO-mediated immune suppression are currently being elucidated, and several positive feedback loops have been identified.

Use of IDO inhibitors in the treatment of chronic infections or cancer may benefit patients by enhancing the intensity as well as the duration of cytotoxic