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## Distinct signal codes generate dendritic cell functional plasticity.

Arima K, Watanabe N, Hanabuchi S, Chang M, Sun SC, Liu YJ

*Sci Signal* 2010 **3**(105):ra4 [abstract on PubMed] [citations on Google Scholar] [related articles] [full text] [order article]

**Selected by** | Bryan D Bell and Steve Ziegler
Evaluated 15 Jun 2010
Relevant Sections

### Faculty Comments & Author Responses

| Faculty Member | Comments |
|---|---|
| Bryan D Bell and **Steve Ziegler**<br>Benaroya Research Institute, USA<br>Immunology<br>New Finding<br>Tech Advance | **This is the first study to show that thymic stromal lymphopoietin (TSLP) activates canonical Jak/Stat and distinct nuclear factor kappaB (NF-kappaB) signalling pathways in human primary myeloid dendritic cells (mDC) in order to promote a T helper 2 response by the immune system.**<br><br>Surprisingly, human TSLP promoted broad and sustained Jak-1 and -2 activation, which further lead to the phosphorylation of Stat-1, -3, -4, -5 and -6. Furthermore, while TSLP signalling led to comparable nuclear translocation of the NF-kappaB subunits p52 and RelB as other activators of mDCs, such as Poly(I:C), R848 and CD40L, it also activated p50, which gives it the unique ability to upregulate OX40L on mDCs. The results presented in this paper further emphasize that proximal and distal signalling events downstream of the TSLPR between mice and humans vary greatly. To date, no evidence has been presented in which murine TSLP requires JAK signalling to activate Stat-5 or exert its biological effects, and no other Stat proteins are phosphorylated in response to mouse TSLP {1}. Lastly, while the authors show that TSLP cannot act as a dominant negative in the suppression of interleukin (IL)-12 signalling in primary human mDCs in response to Toll-like receptor signalling, murine TSLP clearly inhibits lipopolysaccharide-induced IL-12/23p40 production in murine DCs {2}. This study is an important step in determining the molecular mechanisms activated by human TSLP, and it will be very important to determine exactly how human and murine TSLP differ in orchestrating their biological and biochemical effects on the immune system. This will further lead to the ability to develop and test drugs aimed at modulating TSLP signalling in the treatment of atopic diseases.<br><br>References: {1} Rochman and Leonard, Curr Opin Pharmacol 2008, 8:249-54 [PMID:18450510]. {2} Taylor et al. J Exp Med 2009, 206:655-67 [PMID:19273626]. |

**Competing interests:** None declared
Evaluated 15 Jun 2010

How to cite this evaluation

### Faculty Comments & Author Responses

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**1) To cite all the evaluations for this article:**

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Steve Ziegler: Faculty of 1000 Biology, 15 Jun 2010 http://f1000biology.com/article/id/3580968/evaluation

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