

## Skin inflammation is controlled by Jun/AP-1 proteins

**Madrid, 16<sup>th</sup> November 2009** - The journal *Genes & Development* publishes today a cover feature article by Juan Guinea-Viniegra et al. describing a novel mechanism/pathway on how skin inflammation is controlled by the Jun/AP-1 transcription factor complex using different mouse models.

The Genes, Development and Disease Group from the BBVA Foundation-CNIO Cancer Cell Biology Programme, headed by Erwin F. Wagner, has previously linked altered expression of Jun/AP-1 proteins to psoriasis (Zenz, R. et al. *Nature* 2005), a common skin disorder that affects approximately 2% of the population. The causes of this disease likely involve a complex combination of genetic and environmental factors, and there is still no cure for this inflamed, itchy and scaly skin disease.



In this new study, spearheaded by Juan Guinea-Viniegra, the authors show that, as a consequence of Jun/AP-1 deletion and TIMP-3/TNF $\alpha$  deregulation in the epidermis, mice develop a TNF $\alpha$ -dependent skin inflammation. This leads to lethality in newborn mice and to a psoriasis-like phenotype in adult mice. Excessive levels of TNF $\alpha$ , a pro-inflammatory cytokine, play an important role in mediating inflammatory processes and this is of high relevance in human diseases like psoriasis, rheumatoid arthritis and cancer. The new report by Guinea-Viniegra et al. describes the AP-1/TIMP-3/TNF $\alpha$  pathway initiated in the epidermis as a major axis controlling TNF $\alpha$ -mediated skin inflammation which is likely relevant in human diseases, such as psoriasis. Interestingly, this group has also recently shown that blocking VEGF, a key pro-angiogenic factor, dramatically reduces the psoriasis-like symptoms in mice, resulting in almost normal skin (Schonthaler et al. *PNAS* in press). Therefore, these studies reveal possible new targets and avenues for treating inflammatory diseases and possibly cancer.

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