

P057 The effect of disease-causing mutations on the function of the transcription factor IRF6

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Mutations in the gene encoding the transcription factor Interferon regulatory factor 6 (IRF6) cause the human developmental disorders Van der Woude syndrome (VWS) and popliteal pterygium syndrome (PPS). VWS is the the most common syndromic form of cleft lip or palate. Patients with PPS have a similar orofacial phenotype but also exhibit skin and genital anomalies.

The effect of a range of mutations on the structure and function of IRF6 was investigated. We determined the DNA-binding specificity for IRF6 and established that it is a co-operative transcriptional activator. Most, but not all, mutations in the DNA-binding domain abrogate DNA binding. Similarly, most mutations in the transcriptional activation domain inhibit transcriptional activation. The molecular basis for differential phenotypic effects of individual mutations will be discussed.