

*Reg Morgan*

## **The Annexins**

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**Monte Verità, Ascona**

**Annette Draeger, Bern**

**Stephen Moss, London**

**Volker Gerke, Münster**

## 5 REGULATORY MECHANISMS OF ANNEXIN GENE EXPRESSION.

P. FERNANDEZ<sup>1</sup>, S. MARTIN-ALMEDINA<sup>1</sup>, J. JHONCON<sup>1</sup>, R. Morgan<sup>1</sup>

<sup>1</sup>*Biochemistry and Molecular Biology, Faculty of Medicine, University of Oviedo, 33006 Oviedo, Spain*

The regulation of gene expression may ultimately be as important as protein interactions in trying to comprehend and monitor gene function under pathophysiological conditions. We have approached this complex and understudied area of annexin research by first examining global expression patterns and responses for each of the 12 subfamilies in published microarray and proteomic studies. A comparative genomics approach was then used to identify and structurally characterize the individual promoters for each vertebrate annexin over a range of species. These latter data were subsequently subjected to phylogenetic footprinting analysis *in silico* to identify conserved motifs, domains and modules that were most likely to interact with transcription factors and with each other to modulate annexin gene expression. Regulatory models were thus developed for each annexin based on the species conservation of key promoter elements, global expression data, and independent knowledge of the mechanisms in coexpressed genes. This background knowledge provided perspective and insight into putative mechanisms to better focus our experimental work directly on the functional activity of specific promoters. Theoretical working hypotheses formulated for the 12 vertebrate annexin promoters were successfully applied to achieve experimental results elucidating transcriptional control mechanisms involved in the expression of (stomach-specific) annexin A10 and (ubiquitous) annexin A11. Theoretical models and experimental studies of annexin gene expression regulation provide a crucial basis for eventually deciphering the multifunctional profile of these genes.