



## *"Rapidly Evolving Transcription Factors: Investigating Their Role in Shaping Species-Specific Regulatory Networks and Biological Traits"*

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**Donnelly CCBR, Red Seminar Room,**  
**160 College Street**

**Abstract:** Although many transcription factor (TF) genes are highly conserved in structure and function, one large family of TFs is evolving rapidly in vertebrate genomes. This gene family encodes proteins in which a Kruppel-type zinc-finger (ZNF) DNA binding domain is attached to a chromatin-interacting motif, called KRAB, which confers potent repressor activity. KRAB-ZNF genes first arose in tetrapods and have expanded to a family of more than 400 protein-coding loci in the human genome. Continuing rounds of segmental duplication events, coupled with gene loss, have created a significant numbers of lineage-specific genes; for example, only about 100 human loci recognize clear functional orthologs in mouse, and more than 100 human genes of this type correspond to recent primate duplications. New duplicates rapidly acquire structural changes that indicate a drive for creation of proteins with novel DNA recognition properties, suggesting that vertebrate gene regulatory networks are also evolving rapidly. However, the impact of this variation is difficult to assess since regulatory targets have been identified for only a handful of KRAB-ZNF proteins. To address this problem, we are applying a variety of methods to identify gene targets and biological pathways affected by KRAB-ZNF proteins. Our data suggest roles for specific KRAB-ZNF proteins in development, reproduction, immunity and cancer susceptibility, suggesting that gene family expansion has had a significant impact on shaping species-specific and individual human traits.