

GENE-CENTERED PROTEIN-DNA INTERACTOME MAPPING

AJ Marian Walhout

*Program in Gene Function and Expression and Program in Molecular Medicine
UMass Medical School
Worcester, MA*

Transcription regulatory networks play a pivotal role in the development, function and pathology of metazoan organisms. Such networks are comprised of protein-DNA interactions between transcription factors (TFs) and their target genes¹. We are interested in the architecture and functionality of such networks. We developed high-throughput gene-centered methods² for the identification of protein-DNA interactions between large sets of regulatory gene segments and various TF resources, including novel Steiner Triple System-based TF smart pools and a TF array³. So far, we mapped two gene-centered networks using *C. elegans* gene promoters^{4,5}. These networks already provided insights into differential gene expression at a systems level. For instance, we found that most *C. elegans* genes are controlled by a layered hierarchy of TFs that sometimes function in a modular manner. Our data can be accessed in our database, EDGEdb⁶.

1. Walhout, A. J. M. Unraveling Transcription Regulatory Networks by Protein-DNA and Protein-Protein Interaction Mapping. *Genome Res* **16**, 1445-1454 (2006).
2. Deplancke, B., Dupuy, D., Vidal, M. & Walhout, A. J. M. A Gateway-compatible yeast one-hybrid system. *Genome Res* **14**, 2093-2101 (2004).
3. Vermeirssen, V. et al. A *C. elegans* transcription factor array and Steiner Triple System-based smart pools: high-performance tools for transcription regulatory network mapping. *Nat Methods* **In press** (2007).
4. Deplancke, B. et al. A gene-centered *C. elegans* protein-DNA interaction network. *Cell* **125**, 1193-1205 (2006).
5. Vermeirssen, V. et al. Transcription factor modularity in a gene-centered *C. elegans* core neuronal protein-DNA interaction network. *Genome Res* May 18; **[Epub ahead of print]** (2007).
6. Barrasa, M. I., Vaglio, P., Cavasino, F., Jacotot, L. & Walhout, A. J. M. EDGEdb: a transcription factor-DNA interaction database for the analysis of *C. elegans* differential gene expression. *BMC Genomics* **8**, 21 (2007).