

Ratnam Seelan, Ph.D.

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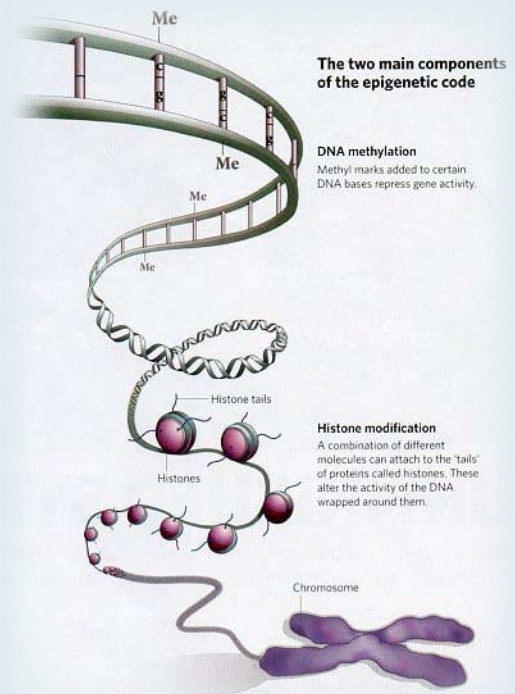
Research Activities:

Dr. Seelan's principal research interests are in understanding the genetic basis of cognitive and neurodevelopmental disorders such as Autism. One area of active interest is to understand the molecular biology of genes involved in *myo*-inositol metabolism such as *myo*-Inositol Synthase and Inositol Monophosphatases 1 and 2. *Myo*-inositol is an important precursor for the 'phosphoinositide signaling' pathway which not only generates IP₃, an important second messenger molecule, but also activates several neuronal receptors required for the normal functioning of the brain. Depleted *myo*-inositol levels are frequently observed in the brains of patients suffering from Autism Spectrum Disorders. Deficiencies in inositol signaling have been implicated in the etiology of several psychiatric disorders including Bipolar Disorder. Specifically, the discovery of novel isoforms for some of these genes in the laboratory has rekindled renewed interest in brain *myo*-inositol synthesis and regulation, subunit composition of the brain enzymes, and identifying the transcription factors that regulate their expression in brain. Much of this work has been done in collaboration with Dr. R. Parthasarathy, VA Medical Center, Louisville. Another area of interest is the epigenetic modulation of these genes in Autism and other behavioral disorders. A role for CpG methylation in brain-specific regulation has been established for some of these genes and CpG



methylation profiles are being developed for normal and affected (Autism) brain tissues to identify critical CpG residues involved in gene expression. Ongoing collaborative studies with Dr. M. F. Casanova, Dept. of Psychiatry and Behavioral Sciences, and Dr. Michele Pisano, Birth Defects Center, University of Louisville, will examine the genetic and biochemical bases for abnormal minicolumns observed in the autistic brain and the effect of

environmental stressors such as maternal cigarette smoke exposure on the cognitive abilities of the offspring. His studies are currently funded by the COBRE mechanism and he continues to seek additional funding support for his varied research interests. Funding from the Department of Defense and March of Dimes grant programs are currently pending.



Grants Funded:

Role: Sub-project Principal Investigator

Title: Effect of interneuron loss on minicolumn structure

Funding Agency: National Institutes of Health/National Center for Research Resources; Center of Biological Research Excellence (COBRE)

Direct Costs Funded: \$120,000

Role: Sub-project Principal Investigator

Title: Regulation of Neural Crest Cell Migration by SDF1-CXCR4 signaling

Funding Agency: National Institutes of Health/National Center for Research Resources; Center of Biological Research Excellence (COBRE)

Direct Costs Funded: \$157,000

Peer-reviewed Publications:

Seelan RS, Khalyfa A, Lakshmanan J, Casanova MF, Parthasarathy RN. Deciphering the lithium transcriptome: microarray profiling of lithium modulated gene expression in human neuronal cells. *Neuroscience* 151: 1184-1197 (2008).