

Distinguished Researcher



- **Name:** Levon Michael
- **Surname:** Khachigian
- **Nationality:** Australian
- **University:** University of New South Wales, Australia
- **Project Title:** Innovative gene-specific “molecular scissors” targeting key genes as potential novel therapeutics in vascular diseases

Abstract

Professor Levon Khachigian, an NHMRC principal Research Fellow, at UNSW's Centre for Vascular research, has been responsible for the creation of ground-breaking paradigm shifts in three main areas of vascular path biology and translational research. First, transcription factor interplay as inducible regulatory circuits in gene expression, as evidenced by landmark papers in *Science*, *EMBO J*, *Circ Res* and *J Biol Chem*. Here, for example, he was the first to identify *Egr1/Spl* displacement initially in the context of platelet-derived growth factor A-chain and B-chain promoters, a circuit which is now recognized as a key mechanism mediating the inducible expression of scores of other pathophysiologically-relevant genes. Second, he has pioneered our understanding of the molecular control of growth and apoptotic genes in cells of injured artery wall. In studies underpinned by papers in *J Clin Invest*, *Circ Invest*, *Circ Res* and 16 papers in *J Biol Chem*, he was the first to link signaling and transcriptional events with vascular cell phenotype in response to changes in microenvironment. Third, and most relevant to this nomination, he has led the international charge in the exciting area of DNAzymes as gene-specific molecular and therapeutic tools, as showcased by papers in *J Natl Cancer Inst*, *Circ Res* and 2 in *Nature Medicine*. He was the first to use DNAzymes in an animal model of any kind and establish key roles for the immediate-early genes *Egr-1* and *c-Jun* in restenosis and angiogenesis. He is now extending this pioneering DNAzyme pre-clinical research into other vascular conditions, such as myocardial infarction, failed bypass grafts, vulnerable plaque and macular degeneration.