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## INTRODUCTION

# Gene Expression in Neuronal Activity

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Molecular Genetics and Neuroscience are converging in a common understanding that neuronal activity influences not only cellular activities such as neurotransmitter secretion and synthesis, but also transcription patterns in the nucleus. Usually, changes in these patterns are brought about by signal transduction pathways that end in the modulation of activity or synthesis of transcription factors. In the chemical senses, there is the opportunity for modulation of gene expression by neurotransmission, and by pathways initiated by external stimuli such as odorants and tastants. Thus, it is timely to examine in detail the rich literature on the modulation of transcription factors, focusing on transcriptional regulation in neuronal cells. Specifically, it seems prudent to focus on two aspects: neurotransmitter control of gene transcription and stimulus-dependent induction of immediate-early genes. A symposium at the Association for Chemoreception Sciences (AChemS XVI) recently addressed these topics and here we focus on papers which discuss regulation of immediate-early genes in general, in neuronal cells and, finally, in the olfactory system.

The immediate early genes are the subject of intense scrutiny because many encode transcription proteins which are pivotal in the conversion of extracellular stimuli into changes in cell phenotype, that is, the genetic program. One of these immediate-early genes, *c-fos*, is described as a 'master switch' which, when activated, mediates signals for growth or differentiation, depending on the specific cell type and the cellular milieu (Verma and Sassone-Corsi, 1987; Herrlich and Ponta, 1989). As Herschman (1991) notes, the studies of mitogenesis, endocrinology, immunology, neurobiology and developmental biology share common

questions about the transduction of extracellular signals into meaningful intracellular ones and eventually into appropriate cellular responses. The remarkable revelations of research indicate that general transduction pathways are the same for most cells. Differences exist primarily at the cell surface receptor and much less so in the intracellular signals, but they virtually all appear to converge on the same immediate-early genes.

Immediate-early gene induction in response to cell stimulation occurs rapidly and without prerequisite protein synthesis (see Angel and Karin, 1991 for review), hence their name. For some of these genes, induction leads to synthesis of transcription factors, such as the Fos and Jun proteins, whose activity is regulated by dimerization and post-translational modification. The active factors then control the transcription of diverse target genes to generate the subsequent phenotypic pattern of expression that constitutes the cellular response. This pathway provides a means for coupling short-term events at the cell surface to long-term changes in gene expression (Morgan and Curran, 1989). Although many immediate-early genes were first identified as oncogenes, it is now appreciated that they also function to control normal gene expression during differentiation and development.

In neuronal cells, the study of immediate-early genes is shedding light on the long-term effects of neurotransmission and the mechanisms by which neurotransmitters can influence post-synaptic gene expression to produce these effects (Esterle and Sanders-Bush, 1991). The patterns of immediate-early gene expression differ with neuronal cell type and stimulus, and the kinetics of induction can vary with the

receptor subtype mediating synaptic transmission (see Esterle and Sanders-Bush, 1991 for review). Even without knowing the detailed cellular mechanisms involved in neuronal immediate-early gene induction, their expression in response to stimulation provides a useful means of mapping activated neuronal pathways (Draganow and Faull, 1989; see Erickson and Millhorn, 1991 for discussion). Such applications are being used in the study of the chemical senses (Guthrie and Gall, 1994; Onoda, 1992).

With the recognition of the roles played by immediate-early genes, we now have a new genetic and biochemical approach to the study of the complex pathways involved in neuronal development, differentiation and long-term responses to stimulation. Some of the major questions which remain concern the identification of transcription factor target genes, the mechanisms involved in regulation of

immediate-early gene products by post-translational modification, and the positive and negative transcriptional activities of the various dimer proteins formed by different members of the immediate-early gene families (Esterle and Sanders-Bush, 1991). As the answers emerge, more light will inevitably be shed on neuronal function.

Because the immediate-early genes figure into so many diverse research areas, cutting edge technology is currently being applied to highly competitive research efforts. Hence, it is important for researchers in AChemS to communicate with scientists who once appeared to be carrying out work unrelated to the field of the chemical senses, and to be cognizant of new technical approaches in the field of immediate-early genes as a whole. We present here four papers on immediate-early genes based on symposium presentations at AChemS XVI in April 1994.

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