A systems biology view about the role of nuclear melatonin receptors in neurogenesis

Joice de Faria Poloni¹, Bruno César Feltes¹, Diego Bonatto¹

¹Institute of Biotechnology, University of Caxias do Sul, Caxias do Sul, Rio Grande do Sul, Brazil, 95070-560

Background

Melatonin (N-acetyl-5-methoxytryptamine) is secreted by the pineal gland in association with supraquiasmatic nucleus (SCN) and controls several metabolic, physiological and behavior processes in different organisms. The synthesis of melatonin is synchronized by the light/dark variation, showing a rhythmic pattern that is evolutionarily conserved. During embryogenesis, the synthesis of pineal melatonin starts postnatally. However, during the embryonic development the fetus shows a rhythmic activity, as the result of a non-photic input signal [1]. The melatonin is one of the few maternal hormones that cross the placenta without being modified [2]. Some studies showed the presence of nuclear melatonin receptors (NMR) in the placenta during the first three months of pregnancy. During the pregnancy, the melatonin level in plasma is kept higher at night than at day in the mother, whereas in the placenta the level of melatonin remains constant [3]. In this sense, the placental melatonin and the SCN-associated maternal melatonin may have distinct functions through NMR during the development of embryo.

Materials and Methods

To clarify the role of NMR in the early embryo development, the interaction between NMR and essential proteins of embryogenesis and neurogenesis was evaluated by means of systems biology tools considering the available protein-protein interaction (PPI) data for Homo sapiens and Mus musculus. For proteomic data mining, the softwares String 8.0 [http://string.embl.de/], iHop [http://www.ihop-net.org/UniPub/iHOP/] and GeneCards [http://www.genecards.org/] were employed. The network topology was evaluated by Cytoscape 2.5.0 [http://www.cytoscape.org/]. The ontology processes were analyzed by the plugins MCODE [http://www.mcode.com.au/] and BiNGO 2.3 [http://www.psb.ugent.be/cbd/papers/BiNGO/], respectively.

Results

Considering the binary PPI network obtained, it was observed an interaction between NMR and BMP4 (bone morphogenetic protein 4), a negative regulator of neural induction [4]. NMR also interacts with SHH protein (sonic hedgehog) that controls the pattern of neurogenesis [5], and with ACVR1 (activin A receptor), which has a role in the differentiation of mesodermal tissues [6]. Interestingly, NMR interacts with the Wnt signaling pathway, a positive modulator of neurogenesis and a negative regulator of BMP4 transcription [4]. The same network topology was observed for both human and murine models, indicating that the action of NMR for embryogenesis and neurogenesis is evolutionally conserved.

Conclusions

According to the results obtained, it can be concluded that the NMR proteins play an important role in differentiation and neurogenesis during the embryonic development.

Acknowledgments

This work was supported by research grants from Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; Grant number 471769/2007-0).

References