Poster

Regulatory elements of VANGL2 expression – Implication in Neural Tube Defects

Cañizares-González, Nuria(1), Jiménez-Medina, Carla (1), Ybot-González, Patricia(1)

(1) Institute of Biomedicine of Seville (IBiS), Campus Hospital Universitario Virgen del Rocío

Avda. Manuel Siurot s/n 41013 Seville

Tutor académico: Smani, Younes

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ABSTRACT

Motivation: Neurulation is a complex process aimed at closing neural tube (NT) that occurs during embryogenesis. It is a highly regulated process which combines molecular and cellular events; if any disturbance happens and the closure is not complete, neuroepithelium remains open and neural tube defects (NTD) appear, which are among the commonest of birth defects. A breakthrough in understanding the basis of neurulation, and thus NTDs, was the discovery of the role of the non-canonical Wnt signalling pathway in this process, which is involved in coordinating cell polarity [1]. Mutations in Vangl2, a member of this pathway, have been linked to human NTDs. While studying Vangl2 regulatory regions in NTDs patients, it was found an alteration in CTCF binding sites. CTCF is a conserved transcription factor expressed ubiquitously which plays a key role during development and in the 3D organisation of the genome. Recently, it has been described that curaxin, a DNA-binding compound with epigenetic abilities, interferes with CTCF expression [2]. The purpose of this work is to elucidate the implication of CTCF on the regulation of Vangl2 expression and consequently on neurulation and the development of the disease.

Methods: The approach was carried out by testing different concentrations of curaxin in vitro (human neuroblastoma cell lines) and in vivo (NTD-mouse model loop-tail, Lp). Lp mice carry a mutation in Vangl2 that causes craneorachischisis in homozygosity and spina bifida in heterocygosity, two types of NTDs [1]. In the in vivo model, the effect of curaxin will be tested in embryo culture in stages previous to the initial NT closure. Analysis studies include gene expression by qPCR, histology and image analysis (Qupath, Cell profiler).

Results: The exposition to curaxin seem to have a negative impact in CTCF expression, afecting indirectly Vangl2 expression. This effect is reflected in vitro, causing an increase in neurites number, in line with previous results [3]; an in vivo, leading to impairments on NT closure.

Conclusions: In conclusion, the results obtained suggest that the diminution in Vangl2 expression that causes neural tube defects could be related to an alteration in one of its transcription factors, CTCF. Nevertheless, the current experiments and more exhaustive studies need to be completed.

REFERENCES

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