Functional characterisation of a novel nucleoporin gene *nup98* in zebrafish embryos

25

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Introduction: The nucleoporin gene *nup98* is important for the regulation of cytoplasmic-nuclear trafficking. Frequent disruptions of NUP98 during chromosomal translocation in acute myeloid leukaemia suggest that it may play a role in normal haematopoiesis. nup98-knockout mice has resulted in early embryonic lethality. Therefore, its role in embryonic haematopoiesis remains unclear. In this study, we have cloned a zebrafish *nup98* gene and examined its role in embryonic development, with particular reference to haematopoiesis.

Methods: Two expressed sequence tags with translated sequence homologous to human NUP98 were identified. The gene was cloned by PCR from cDNA of zebrafish embryos. Expression of nup98 in zebrafish embryos was investigated spatially by whole-mount in-situ hybridisation and temporally by RT-PCR. The functions of nup98 were examined by morpholino knockdown and the effects on embryonic development evaluated by gene expression studies and confocal microscopy. Cellular functions of zebrafish nup98 were investigated in HeLa cells.

Results: Zebrafish *nup98* gene shared 65% identity to human NUP98 homolog in protein sequence. The gene was expressed during early embryonic development since 1-cell stage and diffusely in eyes and the developing brain since 18 hpf. About 30% nup98-knockdown embryos developed intracranial haemorrhage at 48 hpf, resulting from disrupted blood vessels. nup98-knockdown upregulated pu.1 and scl as evaluated by quantitative RT-PCR. Moreover, ectopic expression of zebrafish nup98 rescued the defective mRNA export due to NUP98 knockdown in HeLa cells.

Conclusion: A novel zebrafish *nup98* gene was shown to exhibit conserved function in mRNA trafficking. Its role in embryonic development should be further evaluated.

Declined frontal white matter integrity in Alzheimer's disease: a diffusion tensor imaging study

26

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Introduction: Previous studies on structural changes of Alzheimer's disease (AD) have been focused on grey matter atrophy. There is a resurgence of interests on white matter integrity in this prominently increasing patient population. Diffusion tensor imaging (DTI) provides key information on the microstructural changes beyond macroscopic anatomical imaging by in-vivo tracing molecular diffusion in the brain, and the measured fractional anisotrophy (FA) value may represent axonal integrity of neuronal networks. Data of DTI from AD patients are limited, and the literature is controversial regarding whether the AD process has a greater impact on anterior versus posterior cerebral white matter.

Methods: Eighteen patients with mild AD and 16 age-matched healthy adults were recruited into the study. Demographic features of the two groups were comparable. Data of DTI were collected using a Philips 3.0T MRI scanner. Scan parameters were as follows: B_0=800 s/mm^2, FOV=224*224*140 mm, resolution=1.75*1.75*2 mm, non-collinear 15 directions was acquired. 3D T1 anatomy was also collected. We processed DTI data with DTI toolbox, and anatomical T1 data with VBM5 toolbox in SPM. Voxel-by-voxel analysis was applied to compare the difference in FA value, and volume of white matter of the normalised brain between the elderly and AD groups.

Results: Voxel-based analysis showed no significant difference in white matter volume between the two groups, but FA value was reduced greatly in the left anterior cingulate (–10,37,–3), right anterior cingulate (12,0,28), and left medial frontal lobe (–18,32,–12). Minor reduction was found in other brain regions such as body of the corpus callosum, right midbrain (12,–12,–6), right posterior corpus callosum (8,–44,2), and bilateral, especially right temporal lobe (36,–8,–20), upon right hippocampus. Coordinates (x,y,z) were labelled according to Talairach atlas.

Conclusion: DTI could be valid and more sensitive than traditional T1 anatomy in detecting microscopic white matter lesions. Our data showed a greater decrement in FA value over the anterior than posterior brain regions, and this decrement was not due to white matter atrophy. Our findings are in line with the retrogenesis hypothesis which predicts reversed demyelination during the process of AD, as the frontal lobe fibres are myelinated relatively late during brain development. These results also support previous findings of our behavioural study that frontal lobe abnormality might be the neural basis for cognitive deficit in AD patients.

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