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Vaccination against a generic amyloid oligomer epitope improves cognitive function, reduces plaque and tau pathology in Alzheimer's transgenic mice

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Accumulation of beta-amyloid (Aß) is an important molecular event in Alzheimer's disease (AD). It is now well known that vaccination against fibrillar Aß prevents amyloid accumulation and preserves cognitive function in transgenic mouse models. To study the effect of vaccination against generic oligomer epitopes, Aß oligomers, islet amyloid polypeptide (IAPP) oligomers, random peptide oligomer (3A) & Aß fibrils were used to vaccinate Tg2576 and 3xtg mice which develop a progressive accumulation of plaques, tangles and cognitive impairment. We vaccinated Tg2576 and 3xTg mice monthly with the above mentioned vaccines and studied various cognitive parameters at 6 months, 10 months and 14 months of age. We tested escape latency, number of platform crosses in the Morris water maze test (MWM) (which are related to hippocampus), novel object recognition (which is related to cortex) and inhibitory avoidance (which is related to amygdala). It was found that all vaccinated mice have a significant improvement in cognitive function compared to controls. In addition to cognitive improvement subcutaneous administration of these antigens markedly reduced total plaque load (Aβ burden) and hyper phosphorylated tau (tau pathology). We conclude that amyloid Aß sequence is not necessary to produce a protective immune response as the random peptide (3A) gives rise to an oligomer specific immune response. The critical epitope is a pathology-specific conformation of the peptide backbone that is independent of the specific amino acid sequence. It is therefore suggested that vaccination against a non-human amyloid oligomer epitope may be an effective strategy for developing a vaccine that does not have the potential for auto-inflammatory immune complications.

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Papillary thyroid carcinoma and its variants: The cytolomorphologic features and histologic correlates

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Papillary Thyroid Carcinoma (PTC) is the most common thyroid malignancy. Fine Needle Aspiration (FNA) remains the cost-effective first line diagnostic modality in the evaluation of thyroid lesions. This practical presentation will focus on FNA cytomorphology of PTC variants with the emphasis on its aggressive subtypes. The subtle cytomorphologic differences between the common and aggressive variants of PTC seen in the conventional and liquid-based preparations (LBP) will be analyzed. A case-based approach will be used to discuss the pre-operative diagnosis of more aggressive PTC variants (tall cell, columnar cell, diffuse sclerosing, clear cell, and hobnail). Corresponding ultrasound images, gross and microscopic characteristics of follow-up surgical pathology specimens will be reviewed and correlated. The utility of ancillary studies (immunostains and molecular markers) which facilitate the diagnosis and help to differentiate variants of PTC from other primary thyroid tumors or metastatic malignancies will be addressed. Importance of recognition of aggressive variants of PTC in FNA specimens for the completeness of preoperative planning (total thyroidectomy, possible cervical lymph node dissection and search for distance metastases) will be demonstrated. By the end of this presentation the participants will be able to recognize the differential cytomorphologic criteria of PTC and its variants in the conventional and LBP preparations and effectively integrate clinical data, sonographic features and ancillary tests in the preoperative workup of these lesions.

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