

# What topics are you interested in?

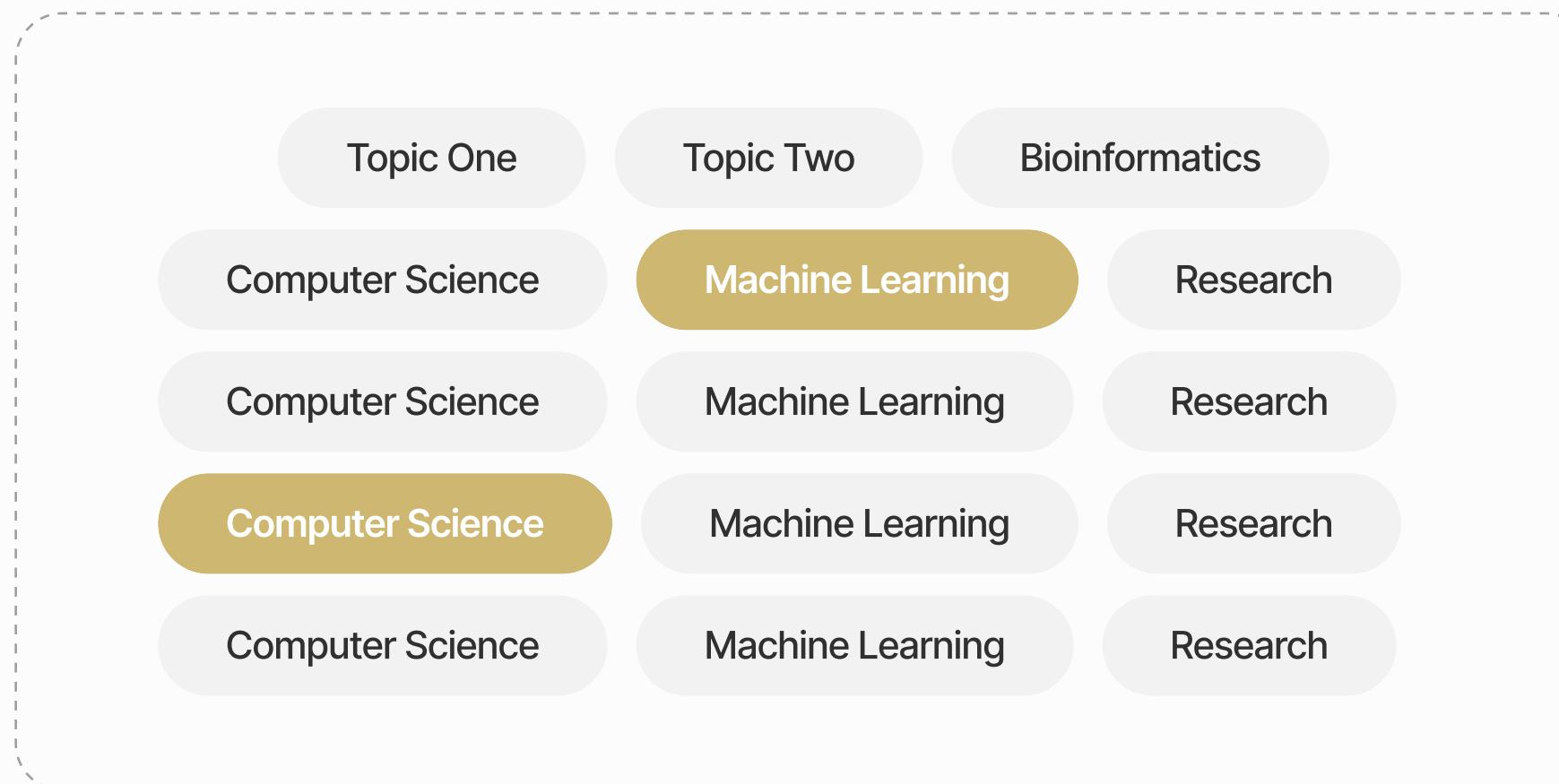
Topic One      Topic Two      Bioinformatics

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Computer Science      Machine Learning      Research

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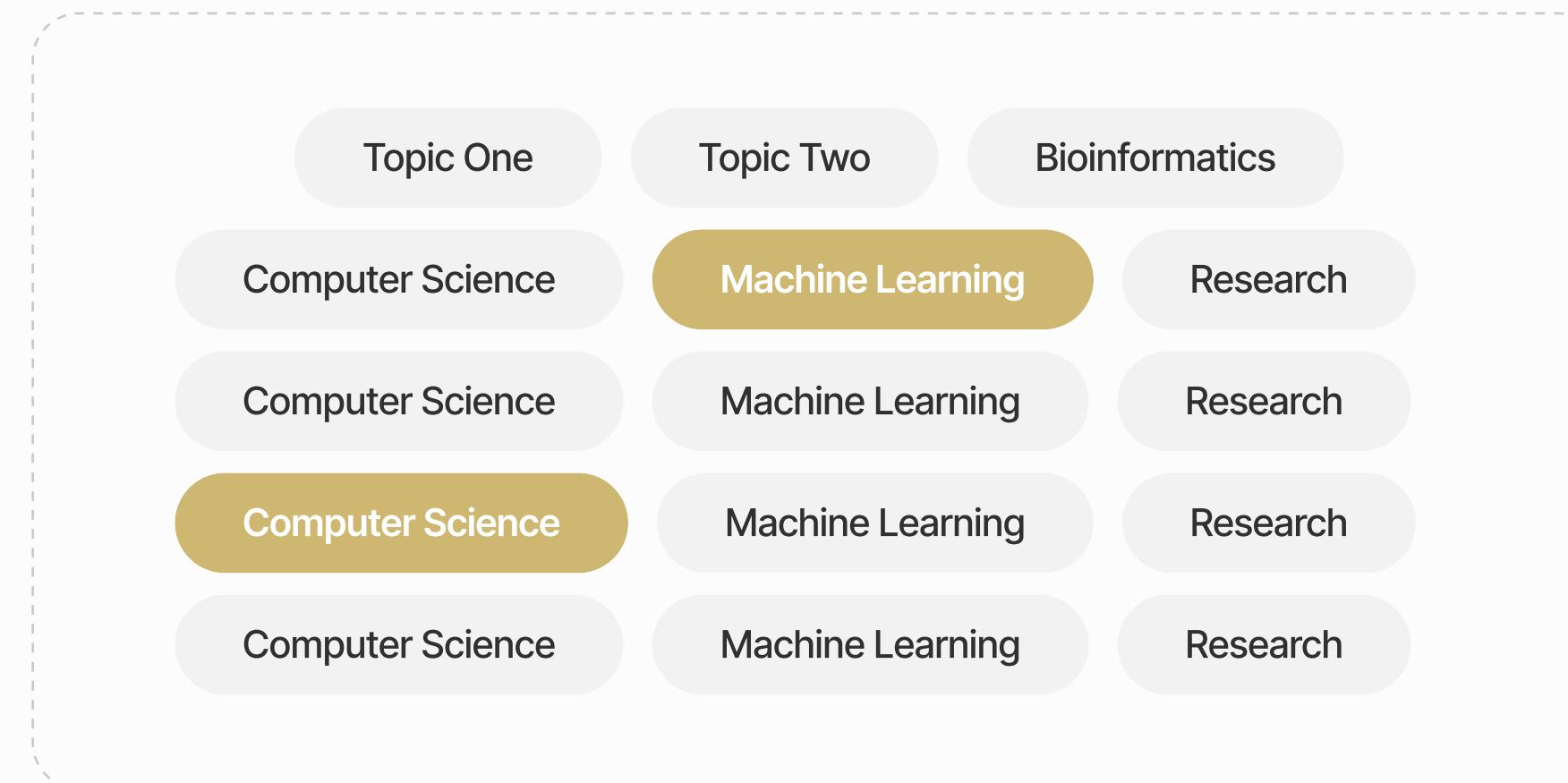
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Sept 12, 2024

## The mechanism and consequences of amyloid- $\beta$ modulating thiamine pyrophosphokinase-1 expression in microglia

Cheng X. · Cheng X.



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Machine Learning

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# The mechanism and consequences of amyloid- $\beta$ modulating thiamine pyrophosphokinase-1 expression in microglia

Ample studies attribute cognitive decline in Alzheimer's disease to amyloid- $\beta$  deposition 1–6. However, brain amyloid- $\beta$  accumulation that saturates years before the manifestation of clinical symptoms is dissociated with cognitive decline of the disease 7. It is unknown how these two processes are mechanistically linked. In this and our accompanied study, we report that thiamine pyrophosphokinase-1 (TPK) deficiency plays essential roles in both processes via distinct mechanisms. Here we describe that diminished microglia Tpk controls the propagation of amyloid- $\beta$  plaques. In APP/PS1 transgenic mice, microglia showed elevated Tpk expression at 2-month-old, but reduction in a plaque-centric manner at 8-month-old. Interestingly, lipopolysaccharide, but not amyloid- $\beta$ , induced Tpk reduction in cultured microglia. Tpk reduction led to microglia dysfunction, showing volatile motility but reduced phagocytosis and weak response to focal tissue injury, with accumulation of intracellular lipid droplets and abnormal mitochondria. In Alzheimer's disease mice, microglia-specific knockout of Tpk caused diminished plaque coverage, exacerbated plaque burden and synaptic loss. However, increased plaques were not accompanied by the development of neurofibrillary tangles or brain atrophy, in contrast to the phenotype described in our accompanied paper with neuronal Tpk deletion. In conclusion, plaque-induced inflammation reduces Tpk in microglia, selectively exacerbating the spread of amyloid pathology.

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# The mechanism and consequences of amyloid- $\beta$ modulating thiamine pyrophosphokinase-1 expression in microglia



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Cheng, X. • Zhao, R. • Qiu, H. • Song, P. • Kou, L. • Sang, S.; Xia, Y.; Cai, W. • Jin, B. • Huang, Q. • Yuan, P. • Zhong, C.

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