

Inside the Bone: How the Marrow Sustains Plasma Cells Over Time

Plasma cells are a key component of humoral immunity. These cells reside in specialised niches within the bone marrow, where their maintenance depends on multiple interactions with surrounding cells and external signals, including cytokines and metabolites. Although the bone marrow plasma cell numbers were previously thought to decline with age, emerging evidence suggests their increase, prompting new questions about how the bone marrow supports them over time. In this study, we investigate how ageing affects the bone marrow environment and plasma cell microniches. Using immunofluorescence imaging, adoptive transfer and co-culture assays, we map plasma cell distribution and identify factors from neighbouring cells that promote their survival. This work aims to reveal how the ageing bone marrow adapts to sustain long-lived plasma cells. Our findings will contribute to a deeper understanding of serological memory and the mechanisms that preserve antibody-mediated protection in older individuals.

4:00 PM | THURSDAY | 22 MAY 2025

●●● **AUDITORIUM, NII**



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Understanding the role of individual domains in the structural stability of human homologs of guanylate binding proteins (GBPs)

The guanylate binding proteins (GBPs) are interferon gamma-inducible large GTPases and play a significant role in innate immunity. Seven human homologs (hGBP1–hGBP7) are known to date, which share high sequence identity. Unlike small GTPases, hGBPs have evolved as multidomain proteins, where the conserved N-terminal globular domain possesses catalytic activity but the extra C-terminal helical domain has a regulatory role in a few homologs. In contrast to the small GTPases, like Ras, which are unstable in their nucleotide-free form, hGBPs are stable without substrates. In this study, we aim to investigate whether the helical domains of hGBPs contribute to protein stability, and to determine whether other domains play a role. To explore this, we performed heat-induced denaturation studies on two closely related homologs, hGBP1 and hGBP2. Surprisingly, they exhibit considerable variation in structural stability. In both cases, overall stability is mainly contributed by the globular domain; however, in hGBP1, the helical domain stabilizes the full-length protein to some extent. On the other hand, in hGBP2, it essentially plays no role in providing overall stability, and the two domains unfold independently of each other. These findings indicate that the helical domain plays different roles in the stability of the two close hGBP homologs, which may have implications for the differences in their biological functions.

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