

**Title:** Clues about the evolution of brains from immunology and robust control

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**Abstract:** To resist infection or cancer, or to clear damage from traumatic injury, multicellular organisms navigate a challenging tradeoff: most mechanisms that can clear unwanted cells or debris will clear some healthy cells as well. Across phyla, this challenge appears to be mitigated either through high cell turnover or through localized defense. By treating immune defense as a robust control problem, we develop theoretical tools to analyze the relationship between regeneration and immunity. The loss of regeneration and acquisition of localized immunity represent a major puzzle in the evolution of vertebrate life, and perhaps a substantial step towards the lifelong maintenance of a cerebral cortex.