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Generation and characterization of mono-specific antibodies to analyze the abundance and function of human granulins

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Background: Mutations in the *GRN* gene induce progranulin (PGRN) haploinsufficiency and are a common cause of frontotemporal dementia (FTD). PGRN is a secreted glycoprotein composed of 7.5 cysteine-rich repetitive domains called granulins (1 through 7) and paragranulin (the half domain). Complete absence of PGRN causes lysosome dysfunction and neurodegeneration, however the precise function of PGRN is still unclear. PGRN is known to be cleaved into granulins, but there is still debate where granulins are made and the precise function of granulins. A major challenge in resolving the function of PGRN and granulins is the lack of specific antibodies. To bridge this gap, we generated novel mono-specific polyclonal rabbit antibodies against each human granulin.
Methodology: Recombinant human granulins (1-7) containing an amino-terminal poly-histidine tag were expressed in *E. coli*, purified, and used to immunize rabbits. Anti-granulin antibodies were isolated using a two-step affinity purification protocol.
Results: Following immunization, rabbit serum was generated that recognized human granulins 1 through 7. Our affinity purification protocol produced mono-specific polyclonal rabbit antibodies that selectively recognized each individual human granulin. Experiments to evaluate the specificity and selectivity of anti-granulin antibodies in cell lines and tissue are ongoing.
Conclusion: We have successfully generated a suite of rabbit antibodies that specifically and sensitively detect endogenous levels of human granulins. These antibodies are valuable tools to investigate the production, abundance, and biological function of PGRN and individual granulins.
Keywords: Progranulin; granulins; antibody; lysosomal storage disease; frontotemporal dementia.

Conflicts of interest

N/A