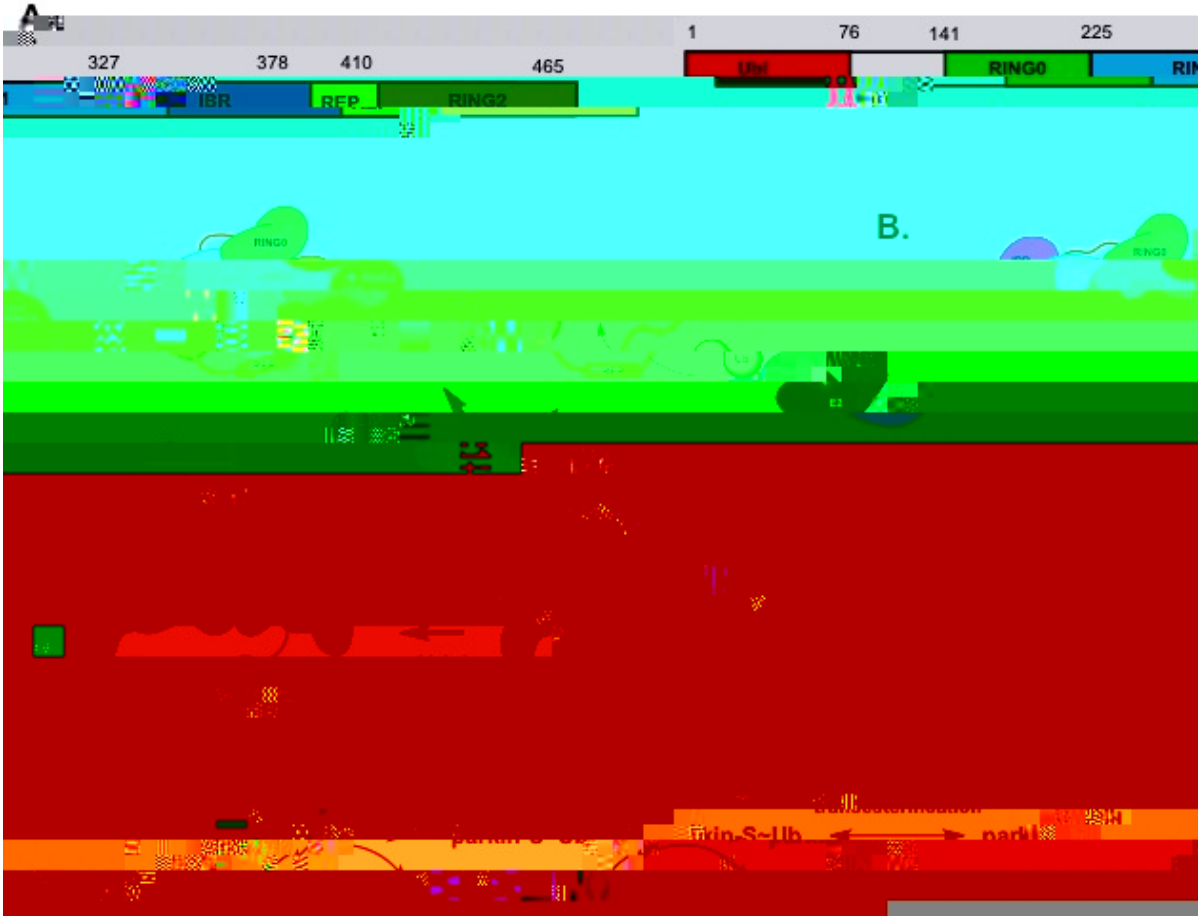
operate together in a pathway that maintains the health and normal function of mitochondria, with parkin likely acting downstream of PINK1[7,8]. Subsequent studies in mammalian cells demonstrated that parkin mediates the engulfment of impaired mitochondria by the autophagy pathway. This is one avenue in which the cell can quarantine and destroy hazardous material from within to protect itself from further damage. For impaired mitochondria, this process is specifically termed mitophagy, and the action of parkin here is dependent on PINK1[9]. Parkin

responding to mitochondrial damage with only a brief delay compared to wild type parkin. By contrast, single mutations that selectively impair the transesterification step of catalysis, for instance a mutation at histidine residue 433, do not detectably slow down parkin recruitment in cells.

Overall, these findings advance evidence that the transthiolation step in parkin catalysis is rate-limiting for the response of this enzyme to mitochondrial distress in cells. The results here suggest that if we are to upregulate parkin activity in PD brains as a neuroprotective strategy, for example with small molecule drugs, the transthiolation step would serve as a robust focus for manipulation. Further elucidation of parkin's role in mitochondrial quality control mechanisms may bring us closer to finding a tool to slow PD progression by helping vulnerable neurons survive. With our continued efforts, we aim to give these neurons the boost they need to halt neurodegeneration in its tracks.



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