

Glucose deprivation causes oxidative stress and stimulates aggresome formation and autophagy in cultured cardiac myocytes

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Aggresomes are dynamic structures formed when the ubiquitin-proteasome system is overwhelmed with aggregation-prone proteins. In this process, small protein aggregates are actively transported towards the microtubule-organizing center. A functional role for autophagy in the clearance of aggresomes has also been proposed. In the present work we investigated the molecular mechanisms involved on aggresome formation in cultured rat cardiac myocytes exposed to glucose deprivation. Confocal microscopy showed that small aggregates of polyubiquitinated proteins were formed in cells exposed to glucose deprivation for 6. h. However, at longer times (18. h), aggregates formed large perinuclear inclusions (aggresomes) which colocalized with γ -tubulin (a

microtubule-organizing center marker) and Hsp70. The microtubule disrupting agent vinblastine prevented the formation of these inclusions. Both small aggregates and aggresomes colocalized with autophagy markers such as GFP-LC3 and Rab24. Glucose de