

Citation (summary) on the outstanding research work on which award is claimed in about 250 words **signed** by the nominator

Exploring mechanisms of neurodegeneration is among the most challenging research areas. Prof. Ganesh has made a pioneering contribution in this field by choosing to dissect the molecular pathways leading to neurodegeneration in a fatal form of a genetic disorder known as Lafora disease (LD). Prof. Ganesh contributed to both understanding the molecular basis of the disease and in applying them for therapeutic interventions. LD, primarily an epileptic disorder, is characterized by the presence of abnormal glycogen inclusions in neurons and is hence often referred to as a glycogen storage disorder. Through a series of publications, his group has demonstrated that, besides the abnormal accumulation of glycogen, the LD brain is defective in autophagy, and that either suppressing the glycogen accumulation or inducing the autophagy reduces neuroinflammation and ameliorates seizure susceptibility in the LD mouse models. His group has also elucidated that a compromised heat shock response pathway leads to neuroinflammation in LD. Some of these leads are being taken to clinical trials. Beyond LD, his group has also demonstrated the role of glycogen synthase (GS) in neuronal autophagy. His findings indicate that GS is activated to induce autophagy when neurons are under stress and that excessive autophagy leads to neuronal death. These findings perhaps explain why neurons usually do not store glycogen, and why degenerating neurons have glycogen accumulation. In summary, Prof. Ganesh has dissected the functional link between complex glycogen metabolic processes and neuronal physiology and provided novel targets for therapeutic interventions.



(Sandeep Verma)