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**Commentary**

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# Customized autophagy: a long way to go

**Jayantee Kalita, Usha Kant Misra, Alok Kumar**

Department of Neurology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Uttar Pradesh 226014, India.

**Correspondence to**: Prof. Jayantee Kalita, Department of Neurology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Raebarli Road Lucknow, Uttar Pradesh 226014, India. E-mail: jayanteek@yahoo.com, jkalita@sgpgi.ac.in

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The survival of any eukaryotic cell may have a unified theory i.e., energy production and clearance of unwanted organelles or pathogens which may be biological or non-biological. Survival of species over time depends not only on survival of cell but also on its ability to replicate and produce progeny. For these functions, intricate genetic, immunological responses including innate and adaptive immunity and congenial environment are needed. Autophagy is one of such mechanism and considered as a housekeeping system of a eukaryotic cell. Takeshige *et al*.[1] in 1990's first time elucidated the underlying mechanism for "autophagy" in yeast and showed that same type of fundamental mechanism is used by cells for degrading and recycling cellular components for which the group leader Yoshinori Ohsumi has been awarded Nobel prize in 2016. In last three decades, the role of autophagy has been extensively studied to understand the pathophysiology and to derive possible treatment options in both acute and chronic neurological diseases such as stroke, trauma, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis *etc*.[2-4]. Recently, the role of autophagy has been evaluated in neuroinfectious diseases especially to understand reactivation of latent virus[5], persistence and replication of RNA virus[6], immune enhancement leading to severe disease manifestations and survival of pathogenic organism against a hostile antibiotic treatment evading its action leading to drug resistance[7]. This review article by Sahu and Ter[8] has reviewed the role of autophagy in central nervous system (CNS) infection.

Amongst the different types of autophagy, macroautophagy is the most extensively studied and well characterized[9,10]. The role of micro-autophagy, chaperon mediated autophagy and xenophagy in central nervous system infections yet to be evaluated for bed side application. The immune regulation in CNS is quite different from systemic immune regulation. CNS mostly depends on microglial mediated immune regulation in presence of normal blood brain barrier and blood-cerebrospinal fluid barrier. However, CNS may suffer from double crash immune dysregulation in presence of CNS infection due to haematogenous

dissemination of virus, bacteria, parasite or fungus, or meningitis in which natural barriers are lost[11]. Autophagy activation in this situation may be due to adaptive immune signalling through pattern recognition or by secretive pro-inflammatory cytokines (for example tumor necrosis factor-α and interferon-γ) following infections[12]. Autophagy can go in both ways, its activation may clear the micro-organism or the micro-organism may use autophagic activation for their benefit and survival[12]. This immune mediated autophagic process is highly regulated by a number of up and down regulating genes[13]. This may be the reason why some organisms provide different disease severity in different individuals or even in the same individual in the subsequent infection. There are many unresolved questions - Does the different organ system have customized autophagy operating system or have uniform operating system? How much autophagy activation is needed for clearance of pathogens and development of protective adaptive immunity? Is it possible to explore the survival autophagy response in adverse situation, the way saprophytic bacteria lives days to years? The resolution of these questions may pave the way for potential new treatment.

## DECLARATIONS

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### Authors' contributions

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Concept, manuscript review: Misra UK
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### Conflicts of interest

There are no conflicts of interest.

### Patient consent

Not applicable.

### Ethics approval

Not applicable.



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