Editorial

Infection tunes stability of key molecules in lung diseases

Keywords

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Lung infection including pneumonia remains one of the leading causes of morbidity and mortality despite advances in treatment and therapy in the past decades. Mounting molecular and cellular studies have revealed that many important proteins are deregulated at the protein level in infectious lung diseases. Either aberrant high level or down-regulation of these proteins is potentially detrimental to the cells that may contribute to the pathogenesis of infectious lung diseases. In the living cells, proteins conducting distinct functions orchestrate together to efficiently fulfill a vast range of life processes. In the processes, proteins are dynamic in responding to the environmental changes. If a given protein is needed, *de novo* synthesis from mRNA will be augmented. Of note, a less emphasized but probably more efficacious way is to enhance the protein stability through preventing from degradation. If redundant, proteins will be promptly dumped out by degradation. Regulation of protein stability via degradation plays an important role in a vast range of life processes. Most proteins destined for turnover are via ubiquity proteasomal/lysosomal degradation machinery. Protein turnover is not a randomly happened event but highly regulated and is a substrate-specific signal transduction cascade. Firstly, targeted proteins are posttranslational modified for recognition by the ubiquitin proteasomal/lysosomal degradation machinery. A well-studied prototype is phosphorylation that may directly affects ubiquitin proteasome system recognition of the substrate. Other posttranslational modifications, such as acetylation, methylation, or palmitoylation are important modifications involved in ubiquitination process as well. Secondly, the destined protein is ubiquitinated. Ubiquitination covalently adds a ubiquitin or polyubiquitin moieties to a lysine residue within the protein substrate. The process of ubiquitination is an enzymatic cascade involving E1 ubiquitin activation enzyme, E2 ubiquitin conjugation enzyme, and E3 ubiquitin ligase. Among the ubiquitin enzymes, E3 ubiquitin ligase recognizes the substrate that is substrate specific. Strikingly, the ubiquitin can be removed from the ubiquitinated protein by a family of enzymes called de ubiquitin enzymes. Finally, the ubiquitinated protein is then escorted into proteasome or lysosome for degradation. Bacterial infection fine-turns proteins involving in cell surface sensors, signal mediator proteins, and effect or proteins. For example, endotoxin lipopolysaccharide treatment or bacterial infection regulates IL22R, IL33, kinases, and TRAF proteins in lung epithelial cells. Epigenetic enzymes that control essential life process such as DNA replication and gene transcription are also deregulated in these models. Enzymes involved in active lung surfactant or other phospholipids synthesis, metabolism, and energy production are also regulated in this system. Understanding the molecular mechanism(s) of protein turnover in infectious lung disease has shed light on the development of new pharmaceutical therapeutic approaches. Successful results have been achieved to screen small molecules against novel molecular targets including E3 ubiquitin ligases in infectious lung diseases.

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Conflict of interest

The author declares no conflict of interest.