

DBT-NII scientists seek to unravel tuning of inflammatory gene response

New Delhi, Sep 22: Inflammation is important for limiting microbial infections; however, there can be aberrations in the process of inflammation, which can cause human ailment, including inflammatory bowel disease and newly emerging COVID-19. Therefore, an improved understanding of inflammatory gene control has profound relevance for human health. Interestingly, various pathogen-derived substances activate a common set of intracellular pathways and yet produce cell-type-selective and stimulus-specific inflammatory gene responses. Although it is known that a defect in this regulatory circuit causes aberrant inflammation, the molecular mechanism involved in context-specific tuning of the inflammatory gene response has not been elucidated.

Focusing on the NF-kappaB signaling system, researchers at the Department of Biotechnology's National Institute of Immunology (DBT-NII) have discussed in a review article on how a handful of intracellular pathways produce such diverse cell-type-selective and stimulus-specific inflammatory responses.



As such, microbial substances activate the canonical NF-kappaB pathway, which induces the nuclear translocation of the RelA:p50 transcription factor. RelA:p50 activates the expression of dozens of inflammatory and immune response genes in multiple cell types. However, this mainstay RelA:p50 transcriptional output is curated, providing for stimulus-type-specific and cell-type-specific inflammatory responses.

They have put forward a conceptual framework where the dynamical attributes and the composition of the nuclear NF-kappaB complexes cumulatively instruct context-specific inflammatory gene patterns. They discuss how dynamical activity of RelA:p50 in the nucleus and context-specific, concomitant activation of non-RelA:p50 NF-kappaB factors eventually instructs the specificity of the inflammatory gene program. They propose that an improved understanding of NF-kappaB mediated inflammatory gene controls may provide specific therapeutic targets in human ailments in the future.

Reference: <https://pubmed.ncbi.nlm.nih.gov>. Online ahead of print.

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Link: <http://www.nii.res.in/>