Decreased IDO1-dependent tryptophan metabolism in aged lung during influenza

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Alterations in mitochondrial gene expression in aged lung during influenza contribute to alterations in metabolic response pathways; specifically, decreased kynurenine pathway mediated tryptophan metabolism and increased ketone body catabolism https://bit.ly/3fb64lF

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ABSTRACT Influenza epidemics remain a leading cause of morbidity and mortality worldwide. In the current study, we investigated the impact of chronological ageing on tryptophan metabolism in response to influenza infection.

Examination of metabolites present in plasma collected from critically ill patients identified tryptophan metabolism as an important metabolic pathway utilised specifically in response to influenza. Using a murine model of influenza infection to further these findings illustrated that there was decreased production of kynurenine in aged lung in an indoleamine-pyrrole 2,3-dioxygenase-dependent manner that was associated with increased inflammatory and diminished regulatory responses. Specifically, within the first 7 days of influenza, there was a decrease in kynurenine pathway mediated metabolism of tryptophan, which resulted in a subsequent increase in ketone body catabolism in aged alveolar macrophages. Treatment of aged mice with mitoquinol, a mitochondrial targeted antioxidant, improved mitochondrial function and restored tryptophan metabolism.

Taken together, our data provide additional evidence as to why older persons are more susceptible to influenza and suggest a possible therapeutic to improve immunometabolic responses in this population.