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Innate lymphoid cells: key drivers of mucosal immunity in COVID-19

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Abstract

Innate lymphoid cells (ILC) may play an important role in innate mucosal immunity. SARS-CoV2 primarily infects the aerodigestive tract. We aimed to compare the frequency and tissue homing tendency of ILC in peripheral blood and stimulated whole mouth fluid (SWMF) in those with and without COVID-19. PBMC and SWMF were processed from 201 individuals: non-infected controls (NIC), asymptomatic COVID (AC); mild COVID (MC); moderate COVID (MOC); post COVID (PC); recovered from COVID (RC) by FACS using anti-human antibodies specific for natural killer (NK) cells, ILC1, ILC2 and ILC3. Frequencies of ILC1 (2.3% vs 0.5/1.0%), ILC2 (0.9% vs 0.1/0.2%) and ILC3 (0.1% vs 0.06/0.006%) were significantly higher in PBMCs of MC compared with NIC/RC. Frequencies of NK cells (15% vs 7.4%), ILC1 (5.9% vs 2.3%), ILC2 (8.1% vs 0.9%) and ILC3 (0.9% vs 0.1%) in MC were significantly higher in SWMF than PBMC, but were not significantly correlated. The frequencies of SWMF ILC1, ILC2 and ILC3 in MC declined over three months to levels similar to RC/NIC, but remained high in SWMF of PC. The tissue retention marker, CD69 and airway homing marker, Integrin α4β1 of ILC were significantly greater in SWMF of MC (ILC1-51%; ILC2-54%; ILC3-47%); but lower in PC (ILC1-48%; ILC2-29%; ILC3-14%). Thus ILC1, ILC2 and ILC3 are elevated during active COVID and declined to normal levels upon recovery; but persist in PC. Increased frequency of ILC in SWMF; not correlated with PBMC; high expression of tissue retention and airway homing markers indicate their role in oral mucosal immunity against COVID-19 for the first time.

Innate lymphoid cells (ILC) may play an important role in innate mucosal immunity. ILC1, ILC2 and ILC3 in SWMF were elevated during active COVID and declined to normal levels upon recovery; but persist in Long COVID indicating their role in oral mucosal immunity against COVID-19 for the first time.

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