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P2737 Beta-glucan in common antimicrobials: inadvertent immunomodulation by trained immunity in surgical prophylaxis and infection treatment

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Background: The fungal cell wall component β-glucan is a potent stimulant of innate immunity. Additionally, recent studies show that β-glucan induces long-term changes in functional programs of innate immune cells, such as monocytes and macrophages. These changes are mediated through epigenetic reprogramming of the cells, leading to increased responsiveness upon secondary stimulation with microbial ligands. This process has been termed trained immunity. It has been described that trained immunity grants nonspecific protection against secondary infections.

Materials/methods: Monocytes were isolated from healthy donor PBMCs and trained with β-glucan, cefazolin, colistin, amphotericin B, ceftazidim, cefuroxim, or itraconazole. Compounds were washed out after 24H and cells were rested for 5 days. The induction of trained immunity was evaluated in terms of the secondary cytokine and chemokine response, the production of reactive oxygen species, killing and phagocytic activity, and induction of glycolysis.

Results: In the present study we demonstrate that commonly used antimicrobial agents, known to be contaminated with β-glucans, induce trained immunity in human monocytes, resulting in increased production of pro-inflammatory cytokines (IL-6, TNF-α) and chemokines (IL-8, MCP-1), and an increase in glycolysis. In addition, host-defence mechanisms such as production of reactive oxygen species (ROS), pathogen phagocytosis and pathogen killing were found to be altered.

Conclusions: These findings identify a parallel mechanism by which antimicrobial drugs contribute to host defence, in addition to their primary antibacterial or antifungal effects. Trained immunity may potentially be applied as prophylaxis for patients at risk for developing infections, such as those with various immune deficiencies, or following surgical intervention. It remains to be determined whether trained immunity is also induced *in \vivo* with these antimicrobial compounds.