P2306 Transketolase and vitamin B1 influence on Staphylococcus aureus-mediated neutrophil extracellular traps formation

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\textbf{Background:} Neutrophil extracellular traps (NETs) are a novel antimicrobial mechanism of neutrophils composed of releasing nuclear DNA and antimicrobial proteins to entrap and kill microbes. NETs are extruded into the extracellular environment via the reactive oxygen species (ROS)-dependent cell death pathway. Transketolase (TKT), a thiamine pyrophosphate (vitamin B1)-dependent enzyme, belongs to the NET-associated protein localized in the cytoplasm of neutrophils. In the present study, we investigated the impact of TKT and vitamin B1 on \textit{S. aureus}-mediated NETs.

\textbf{Materials/methods:} Firstly, TKT was selected from 24 NET-associated proteins obtained by literature screening and knowledge gap assessment (or Big data to knowledge process). The role of TKT and vitamin B1 on \textit{S. aureus}-mediated NETs were consequently addressed \textit{in vitro}. Human purified neutrophils were preincubated with increasing concentrations of oxythiamine, a TKT inhibitor, or vitamin B1 following stimulation of \textit{S. aureus} at a multiplicity of infection (MOI) of 10. The amounts of NETs were measured using a fluorometric double-stranded DNA quantification and the ROS levels were measured by flow cytometry.

\textbf{Results:} Among 24 known NET-associated proteins, TKT was selected as a lead candidate for follow on investigation based on: 1) The relative under-representation of TKT in the body of literature on NETs and 2) The observation in transcriptome datasets of significant changes in TKT abundance during infectious. Interestingly, three independent transcriptome datasets strongly revealed a significant expression of TKT transcript in \textit{S. aureus} infection compared to healthy control, suggesting that TKT might be involved during \textit{S. aureus} infection. \textit{In vitro} studies, we found that oxythiamine or vitamin B1 treatment exerted a significant suppressive effect on the amount of NETs and ROS production in \textit{S. aureus} infection.

\textbf{Conclusions:} Treatment of TKT inhibitor or vitamin B1 could modulate a significant inhibition of ROS-dependent NET activity. It should be alternatively recommended for an adverse pathological outcome in excessive NET formation such as severe sepsis or auto-inflammatory diseases.