Exploring the potential of a pneumococcal vaccine to target oxidized LDL in metabolic disease patients

Lipid metabolism involves a wide range of processes in which lipids are processed and used as energy sources, signaling molecules and structural elements of cells. Given its importance, dysfunctions in lipid metabolism, both small and large, can have significant negative effects for the body. In line, there is a wide range of lipid disorders and diseases which increase the risk of developing fatal diseases such as liver and cardiovascular disease and cancer. Importantly, due to the rise of the so-called Western lifestyle, characterized by excessive caloric consumption and low energy expenditure, an alarming and increasing number of people develop lipid-associated disorders and metabolic diseases. As such, it is now more important than ever to develop effective strategies to prevent and treat metabolic diseases.

Among other events, increased production of oxidized low-density lipoproteins (oxLDL) is emerging as an important bridge between lipid metabolism dysfunction and development of metabolic diseases. After meals, the liver processes and packages a variety of lipids as LDL particles, which it then sends into the circulation so that these lipids can be delivered to other tissues and organs for their use. In patients with lipid disorders and metabolic diseases, disturbed cell function leads to inflammation and oxidative stress, leading to the modification of a variety of molecules, including the conversion of LDL into oxLDL. Unlike LDL, the uptake of oxLDL by cells leads to further cellular dysfunction, inflammation and oxidative stress, exacerbating a pathogenic vicious cycle that can both trigger and worsen metabolic diseases. Previously, researchers showed that by injecting mice with inactivated *S. pneumoniae*, a bacterium known for inducing lung and brain disease, they can induce the production of antibodies against phosphorylcholine (PC), a component of *S. pneumoniae* and of oxLDL. By increasing antibody levels against PC, researchers were able to increase the clearance of oxLDL and improve disease severity in animal models for atherosclerosis, non-alcoholic liver disease and Niemann-Pick disease, suggesting that pneumococcal immunization is a promising tool to target oxLDL.

In order to analyze whether pneumococcal vaccine also increases antibodies against PC and/or oxLDL in humans, we conducted a pilot clinical trial in patients with metabolic diseases characterized by lipid metabolism dysfunction, inflammation and oxidative stress, namely patients with familial hypercholesterolemia, partial lipodystrophy and Niemann-Pick disease. Four weeks after receiving one dose of Prevenar 13, a pneumococcal vaccine commonly used in the clinic, we did not observe an increase in patients' antibody levels against PC and/or oxLDL. While larger studies are necessary to confirm our findings, our results suggest that a single dose of Prevenar 13 is not suitable to increase antibodies against PC and/or oxLDL. As such, further research is required to develop efficient immunization strategies to target oxLDL in humans.

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