O080

1-hour Oral Session

Vaccination: experimental and clinical correlates

Vaccine efficiency against meningococcus in a humanized mouse model

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Objectives:

Due to the severity of meningococcal infections, preventive strategies are urgently needed. Thus far, the difficulty was the absence of relevant *in vivo* models of infection owing to the human specificity of this pathogen. To overcome this, our laboratory designed a humanized mouse model by xenografting human skin into SCID/Beige mice which reproduces the key histological features of purpuric lesions. Here, we aimed to test vaccine efficiency into this humanized model of infection, and validate the model to test preventive strategies.

Methods:

We choose a conjugate quadrivalent vaccine, Menveo®, active on A, C, Y and W135 serogroups. We generated sera with active immunization of CD1 immunocompetent mice. One group was injected at day 0, day 14 et day 28 with Menveo® called "Menveo® group", and control group with phosphate buffered saline (PBS) solution "PBS group", in the same way. At day 42, we sacrificed CD1 mice and collected the sera.

Human skin was grafted onto SCID/Beige mice as previously described. We immunized humanized mice passively: one group with sera obtained from "Menveo® group" called "Menveo® SCID", and control with sera obtained from "PBS group" called "Control SCID". Then, we infected all animals with the 8013 MenC strain. Blood and tissue CFU counts were determined 6 hours post-infection. Histological analysis of tissue was performed on all samples to detect inflammation, coagulation and vascular damage.

Results:

After passive immunization, bactericidal antibodies activity was as fast as 5 minutes and significant difference increased after 6 hours in "Menveo® SCID" group compared with "Control SCID" group. Furthermore, CFU counts were lower in human tissue in "Menveo® SCID" group than in "Control SCID" group. Histological analysis reveals reduced vascular damage and inflammation in the "Menveo® SCID" group.

Conclusion:

For the first time, we showed in an *in vivo* model of infection the efficiency of a vaccine against meningococcus. It induced a significant difference compared to controls in terms bacterial count in the blood and tissues, as well as reduced tissue damage. This humanized model is appropriate for assessing meningococcal vaccines. The xenografting model will be tested in the coming months to assess Bexsero® vaccine efficiency against serogroup B.