Docket #: S18-469

BROADLY NEUTRALIZING ANTIBODIES AGAINST DENGUE VIRUS

Researchers at Stanford and the Chan Zuckerberg Biohub have discovered cross reactive, broadly neutralizing human antibodies against all serotypes of dengue virus.

Dengue virus (DENV) is transmitted to humans through mosquitos and causes approximately 400 million global infections each year. DENV has four antigenically distinct serotypes (DENV 1-4), and reinfection with a heterologous DENV serotype is a risk factor for developing potentially fatal severe disease. This increased risk is partially due to the prevalence of cross-reactive antibodies from the initial infection that can bind to but not neutralize the secondary viral serotype and instead causes antibody-dependent enhancement and disease enhancement. Furthermore, there is no approved antiviral treatment for dengue infection. Therefore, it is desirable to create a DENV therapeutic, or vaccine, which can elicit broadly neutralizing antibodies (bNAbs) against all DENV serotypes simultaneously.

Stage of Research
The inventors have identified cross-reactive neutralizing antibodies from DENV-infected individuals. The inventors leveraged bioinformatics-based analyses of clonally expanded and somatically hypermutated B cells to focus their screen for candidates which are likely to produce antigen-specific and affinity-matured antibodies. Through single-cell transcriptomics of cultured peripheral blood mononuclear cells (PMBCs) of both dengue patients and healthy individuals the inventors discovered neutralizing monoclonal antibodies which exhibit broad neutralization of all DENV serotypes.

Applications

- Pharmaceutical treatment of dengue virus

- Diagnostic identification of dengue virus infection

Advantages

- Antibodies and antigen binding portions thereof which can specifically recognize, and broadly neutralize, all DENV serotypes

Publications

- Durham ND, Agrawal A, Waltari E, Croote D, Zanini F, Davidson E, Fouch M, Smith O, Carabajal E, Pak JE, Doranz BJ, Robinson M, Sanz AM, Albornoz LL, Rosso F, Einav S, Quake SR, McCutcheon KM, Goo L. Functional characterization and lineage analysis of broadly neutralizing human antibodies against dengue virus identified by single B cell transcriptomics. bioRxiv doi: 10.1101/790642 (2019).

Patents

- Published Application: WO2020033491
- Published Application: 20210188948
- Issued: 12,161,890 (USA)

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