

A CLINICALLY VALIDATED *DROSOPHILA* S2 BASED VACCINE PLATFORM FOR PRODUCTION OF MALARIA VACCINES

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Drosophila S2 insect cell expression is less known than the extensively used *Spodoptera* or *Trichoplusia ni* (Hi-5) insect cell based Baculovirus expression system (BEVS). Nevertheless it has been used in research for almost 40 years. The cell line was derived from late stage *Drosophila melanogaster* (Fruit fly) embryos by Schneider in the 1970s, who named the cell line *Drosophila* Schneider line 2 (synonyms: S2, SL2, D.mel. 2). The system has been widely applied to fundamental research, where the availability of the whole genome sequence of *Drosophila melanogaster* (1, 2) and the S2 cells' susceptibility to RNA interference methods (3, 4) have enabled genome wide RNAi screening and whole genome expression analysis techniques to be used to great effect. S2 cells have proved to be highly effective for the production of proteins from a great variety of protein classes (5), such as: viral proteins, toxins, membrane proteins, enzyme, etc. Recent publications have also shown the strength of the S2 system in expression of Virus Like Particles (VLPs) (6).

ExpreS²ion has developed the ExpreS2, *Drosophila* S2 platform to achieve improved yields for difficult to express proteins. Furthermore, several technologies have been developed to improve the ease of use of the system, as well as enable fast and efficient screening of multiple constructs.

S2 based production processes for two malaria vaccine clinical trails with The Jenner Institute, Oxford University (Rh5 (7,8), blood-stage malaria) and Copenhagen University (VAR2CSA (9) pregnancy associated malaria) have been developed. The placental malaria vaccine is currently in a phase Ia trial in Germany, and a Phase Ib trial in Benin. The blood-stage malaria vaccine is currently in Phase IIa trial and is expecting results by the end of 2018.

Several transmission-blocking candidates have been identified over the years with some of the most prominent being pfs48/45, Pfs230C and Pfs25(10). Other vaccine targets focus on blood-stage malaria such as Rh5, PfPRIPR and CyrPA. We will present data on the development of a high producing Pfs25 monoclonal cell line and the purification from said cell line, as well as expression data on a range of other malaria vaccine targets. This present the clinically validated ExpreS2 platform as a complete system for a wide range of malaria targeting vaccines.

(1) Adams M.D. et al. Science 2000 287:2185-2195

(2) Ashburner M, et al. Genome Res. 2005 Dec;15(12):1661-7

(3) Neumüller RA, et al. Wiley Interdiscip Rev Syst Biol Med. 2011 Jul-Aug; 3(4):471-8

(4) D'Ambrosio M.V. et al. J. Cell Biol. Vol. 191 No. 3 471-478

(5) Schetz J.A. et al. Protein Expression in the *Drosophila* Schneider 2 Cell System, Current Protocols in Neuroscience, 2004

(6) Yang L. et al. J Virol. 2012, Jul;86(14):7662-76.

(7) Wright K.E. et al. Nature, 2014 Nov 20;515(7527):427-30

(8) Hjerrild K.A. et al. Sci Rep. 2016 Jul 26;6:30357

(9) Nielsen M.A. et al. PLoS One. 2015 Sep 1;10(9):e0135406

(10) Chaturvedi N et al. Indian J Med Res. 2016 Jun;143(6):696-711