

NRC Institute for Biological Sciences
**Human Soluble VH and VL Single-Domain
 Antibody Libraries for Human Therapeutic Applications**

The Business Opportunity

Camelid VHH and shark VNAR single domain antibodies have the drawback of being immunogenic because of their non-human nature. This limits their applications in human therapy. Fully human VH and VL single domain antibodies would be ideal molecules for human therapy because of their expected lower (or lack of) immunogenicity. However, since they are generally insoluble, methods need to be developed to select non-aggregating domains of the antibody molecule. Non-aggregating human single domain antibodies would possess all the desirable properties of naturally occurring ones, with the added advantage of being non-immunogenic so they may be applicable to a broad spectrum of therapeutic applications, e.g. cancer or infectious diseases.

The Technology

The invention addresses the exceedingly large size and/or poor biophysical properties such as low stability, irreversible unfolding and low expression and, therefore, limited clinical applications of human conventional antibodies and antibody fragments.

The NRC-IBS patent application discloses:

- a selection method for the isolation of non-aggregating binders from phagemid vector-based single-domain antibody phage display libraries, and
- two novel randomization strategies that:
 - make VH synthetic libraries a good source of enzyme inhibitors and binders to cryptic sites and
 - increase the proportion of non-aggregating VHs and VLs in synthetic VH libraries.

Patent Position

Patents Pending – NRC IBS cases 11686 and 11965

Contacts

Stacey Nunes
 Tel.: (613) 993-9212
 Business Relations
 E-mail: stacey.nunes@nrc.gc.ca

Dr. Yves Geoffrion
 Tel.: (613) 991-6377
 Business Relations
 E-mail: yves.geoffrion@nrc.gc.ca

Key Publications

Arbabi-Ghahroudi M, Mackenzie R, Tanha J. *Selection of Non-aggregating VH Binders from Synthetic VH Phage-Display Libraries*. *Methods Mol Biol*. 2009;525: 1-30.

Arbabi-Ghahroudi M, To R, Gaudette N, Hiramata T, Ding W, MacKenzie R, Tanha J. *Aggregation-resistant VHs selected by in vitro evolution tend to have disulfide-bonded loops and acidic isoelectric points*. *Protein Eng Des Sel*. 2009 22: 59-66.

To R, Hiramata T, Arbabi-Ghahroudi M, MacKenzie R, Wang P, Xu P, Ni F, Tanha J. *Isolation of monomeric human V(H)s by a phage selection*. *J Biol Chem*. 2005 280: 41395-403.

The Market

MABs are highly sought after by the pharmaceutical industry to fill their pipelines with new biologics. Pharmaceutical companies are equally interested in upcoming biologics, MABs in particular. Therapeutic monoclonal antibodies are used to treat wide range of diseases, from cancer to rheumatoid arthritis.

Market size:

European therapeutic monoclonal antibody market estimated revenues (2007) of \$7.9 billion, increasing in 2014 to \$22.2 billion. (2007-2014 market growth rate (CAGR) 15.9%)

U.S. therapeutic monoclonal antibodies market estimated revenues (2007) of \$12.6 billion, increasing in 2014 to \$34.5 billion (2007-2014 market growth rate (CAGR) 15.4%)

Source: Frost & Sullivan 2008 All figures are rounded.

Technology Transfer Possibilities

- A commercial exploitation license for the technology.
- Development of this technology through a joint collaboration.