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Construction and usage of large antibody libraries in mammalian cells

Michael R Dyson, IONTAS Ltd, UK
IONTAS Ltd, UK

The availability of large libraries of binders expressed within mammalian cells will allow direct screening for function through simultaneous expression and functional reporting within the same cell. In addition, libraries of binders in mammalian cells could also be used for display of binders on the cell surface allowing the screening of millions of clones by flow sorting while providing information on both the level of expression and the extent of binding within individual clones. The main limitation in achieving this has been the inability to construct sufficiently large libraries containing a single antibody gene/cell. We have solved this problem by directing the integration of antibody genes into a single genomic locus through the use of site-specific nucleases. Antibody libraries consisting of many millions of clones have been constructed and binders selected. This includes antibodies formatted as IgGs expressed in the cell type used for production.

jmc@iontas.co.uk

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