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1. Introduction

Neisseria meningitidis

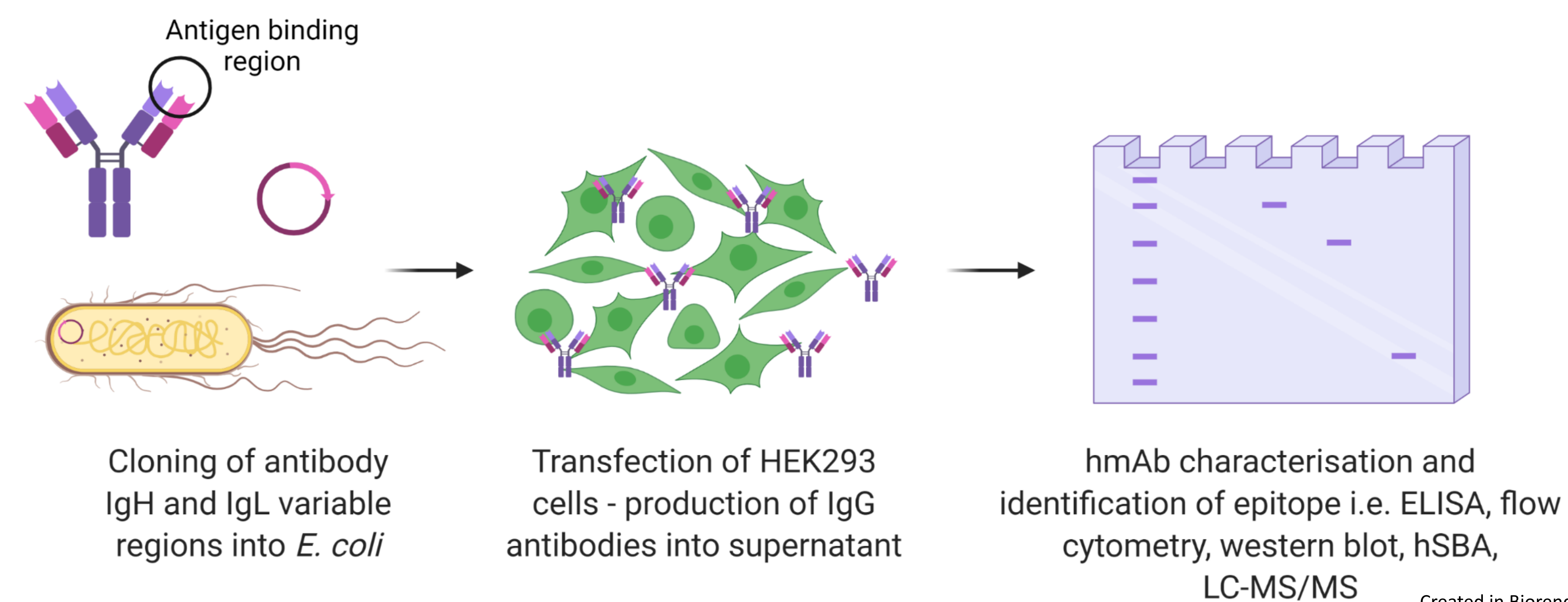
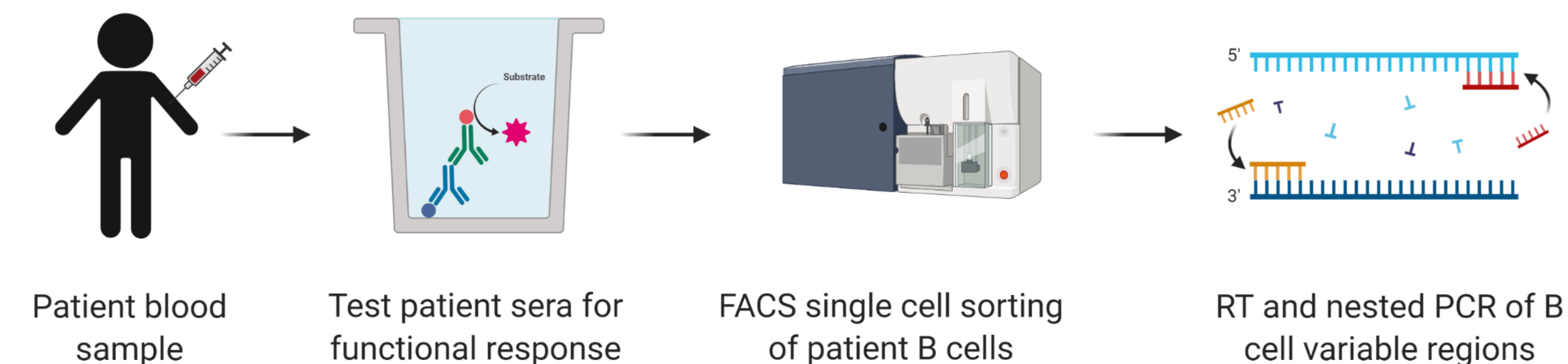
- The most common cause of bacterial meningitis and septicaemia in the UK
- 10% of infections are fatal
- 25% of survivors have long term effects

Current vaccines

- Effective conjugate vaccines against *N. meningitidis* serogroups A, C, W and Y
- Effective recombinant protein vaccine (Bexsero) licensed against serogroup B in the UK in 2013
- Strains of serogroup B protected against by this vaccine vary worldwide:
 - **91%** in USA, **70%** in England and Wales, only **37%** in Argentina

New vaccine antigens could be used to extend strain coverage and increase protection against meningitis

2. Reverse Vaccinology 2.0



3. Results

- **35 anti-meningococcal human monoclonal antibodies (hmAbs)** cloned from six patients
- These antibodies had binding to *N. meningitidis* tested using **ELISA** and **flow cytometry**, before the size of their target protein was assessed using **western blot**
- A selection went on for testing of functional activity:
 - **Serum bactericidal assay (SBA)** tests if an antibody kills *N. meningitidis* when combined with human complement
 - **Complement deposition assay (CDA)** assesses whether the antibody (when bound to *N. meningitidis*) can recruit complement components C3c or C5b-9
 - C3c is an opsoniser which labels the bacteria for killing by phagocytes
 - C5b-9 is a complex which causes bacterial lysis and therefore bacterial killing
- Here we highlight the results from **five promising antibodies**

Antibody	Immunoassays		Target size (kDa)	Functional assays		
	ELISA and flow cytometry	Western blot		SBA	CDA: C3c	CDA: C5b-9
P02-1A1	Green	Green	30 - 40	Green	Green	Green
P02-5A2	Green	Red	ND	Red	Green	Green
P02-5E10	Green	Green	30 - 40	Green	Green	Red
P09-2F2	Green	Green	20-30	Red	Green	Green
P09-2F7	Green	Red	ND	Red	Green	Green

Green boxes indicate a positive result, whilst red boxes indicate a negative result. ND = no data available

4. Conclusions

- To date we have cloned 35 hmAbs that bind to one or more strains of *N. meningitidis*
 - Some antibodies, including P02-1A1 and P09-2F2, bind to a wide range of *N. meningitidis* strains
 - So far, three antibodies have shown SBA activity, with nine hmAbs recruiting human complement C3c and/or C5b-9 in CDA
 - Five antibodies have had their target antigen size identified through western blot
- Future work will focus on further characterisation of all 35 hmAbs, and identifying the target antigens, before assessing these as vaccine candidates

Acknowledgements: PhD funding from BBSRC NPIF (National Productivity Investment Fund) in collaboration with GSK Vaccines Siena.