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DEVELOPMENT OF AN AUTOMATED MICROSCALE PLATFORM FOR CONJUGATE VACCINE PRODUCTION IN *E. coli*

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The current state-of-the-art for the production of glycoconjugate vaccines is a lengthy and complex series of process steps. An exciting alternative is Protein Glycan Coupling Technology (PGCT), where glycoconjugates are produced *in vivo*\(^1,2\). This offers a significant reduction in the time and cost burden of glycoconjugate production, making this technology much more feasible for providing vaccines in developing countries. Current research seeks to apply this technology for pneumococcal vaccines \(^2\), however much process optimisation must be done before this is achievable. This work seeks to provide an automated screening platform at the microscale, enabling the rapid screening of different process variables at considerably smaller volumes.

Scaling was performed based upon oxygen mass transfer\(^3,4\), whereby engineering correlations were used to estimate the value for \(k_{L}a\) in both falcon tubes (bench scale production) and microwells (scale down platform). This provided a good match in cell culture performance and enabled the development of a microscale platform amenable to automation.

Using a combination of feedback loops and executable commands, the automated platform developed showed robust and consistent performance in both cell growth and product expression, with fully hands-free operation. The automated platform was then successfully used for a number of screening studies, identifying the best producing engineered *E.coli* strain for the glycoconjugate vaccine, an efficient induction protocol and the best carrier protein constructs \(^5\).

Exponentially determined \(k_{L}a\) values were then used to scale up the microscale platform to a bench-scale bioreactor culture. This proved the relevance of the data gathered at the microscale to bioreactor cultures and demonstrated the successful transition from shaken to stirred agitation with identical product expression.

This work sought to develop an automated screening tool for ongoing glycoconjugate vaccine development. Thus far, the automated platform has been used in a number of screening studies and has proven scalability with a bench-scale bioreactor culture process. Continued work seeks to optimise a defined media protocol with more rigorous downstream processing to progress this vaccine candidate toward Clinical Phase I trials.

References