Summary project results: 'Pathogenicity of human antibodies cloned from Guillain-Barré syndrome patients.'

In approximately half of the patients with Guillain-Barré syndrome (GBS) particular antibodies can be detected in the blood. These antibodies recognize molecules that are present in nerves and cause nerve dysfunction but how this happens exactly is unknown. In a previous study we revealed the DNA code of one antibody derived from a patient with GBS. This allowed us to produce high quantities of pure antibody in the laboratory and to investigate the detailed binding characteristics to both the eliciting agent, the bacterium *Campylobacter jejuni*, and nerve cells.

An important finding of the study is that the purified antibody indeed strongly binds to *C. jejuni*. A unique aspect of the methodology was the use of the bacterial strain isolated from the very same patient. The purified antibody also recognized human stem cell-derived motor neurons. On a molecular level we observed that the binding strength was much lower to the host neuronal molecules as compared to the bacterial molecules, which are slightly different in structure. This might explain why *C. jejuni* is capable of inducing an immune response that at the same time cross-reacts with nerve tissue. The blood serum of the corresponding patient showed a broader pattern of reactivity, suggesting the presence of several distinct antibodies in the blood of one patient.

Interestingly, we observed that the purified antibody bound better to its target in the presence of another molecule. This phenomenon has previously been described in vitro using blood serum. Our results suggest that the increased binding is not simply due to the fact that serum contains a mixture of antibodies, but that it can be a feature of the antibody itself. The additional molecule was however not required for the binding of the purified antibody to nerve tissue. It is possible that other molecules have similar effects and compensate for the lack of this particular molecule in the tissue.

In conclusion, our study demonstrates that purified patient-derived antibodies provide novel insight into the mechanism by which antibodies develop and cause GBS. Further research is needed to clarify the consequences of antibody binding to nerve tissue and to develop more patient-derived antibodies in order to extrapolate the findings to GBS in general.

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