

Bonvin P, Venet S, Fontaine G, Ravn U, Gueneau F, Kosco-Vilbois M, Proudfoot AE, Fischer N. (2015). De novo isolation of antibodies with pH-dependent binding properties. *mAbs*, 7(2):294-302.

pH-dependent antibodies are engineered to release their target at a slightly acidic pH, a property making them suitable for clinical as well as biotechnological applications. Such antibodies were previously obtained by histidine scanning of pre-existing antibodies, a labor-intensive strategy resulting in antibodies that displayed residual binding to their target at pH 6.0. We report here the de novo isolation of pH-dependent antibodies selected by phage display from libraries enriched in histidines. Strongly pH-dependent clones with various affinity profiles against CXCL10 were isolated by this method. Our best candidate has nanomolar affinity for CXCL10 at pH 7.2, but no residual binding was detected at pH 6.0. We therefore propose that this new process is an efficient strategy to generate pH-dependent antibodies.