



THE ANTIBODY CONUNDRUM

A HISTORICAL TIMELINE OF Ab QUALITY

Oct. 2003: The *Journal of Comparative Neurology* becomes the first publication to set up a policy of requiring extensive validation data on each antibody. Dr. Clifford Saper, editor-in-chief of *JCN*, begins curating an antibody database.

Oct. 2008: Study published in *Molecular & Cellular Proteomics* by Berglund et al. validated 5436 routinely used commercial antibodies from 51 providers and found that half of the antibodies failed established quality standards.

Jan. 2011: T. A. Egelhofer publishes an evaluation of 246 antibodies used in epigenetic studies and finds that 25% failed tests for specificity.

Mar. 2012: Controversial study co-authored by C. Glenn Begley published in *Nature* notes that researchers were unable to replicate 47 of 53 landmark preclinical studies.

2014: WuXi AppTec subsidiary Abgent tests their antibodies and subsequently discards approx. one third of their catalogue.



Mid-2014: Proteintech begins using small interfering RNA to knock down gene expression in novel antibody products.



Feb. 2015: Andrew Bradbury, along with 110 co-signatories, publishes an article in *Nature* calling for an international collaboration and funding initiative to define all binding reagents according to the sequences that encode them, estimating that roughly \$1B would be required to generate characterised recombinant binding reagents to target the primary products of all 20,000 human genes.

June 2015: Bio-Rad launch new line of antibodies that have been tested for off-target activity in western blots against 12 different cell lines.



Sep. 2015: Abcam introduces knockout (KO) validation at scale, using human KO cell lines generated from haploid cellular models employing CRISPR/Cas9 in order to facilitate the development of an increasing range of KO-validated antibodies, including many recombinant monoclonals. Mathias Uhlen, a protein researcher at the Royal Institute of Technology in Stockholm, chairs the inaugural meeting for a working group on antibody validation hosted by the Human Proteome Organization.

Oct. 2015: Abcam develop a mAB production platform from rabbits, stating that the platform is much more specific immunochemical alternative to traditional mice/rat equivalents.



Jan. 2016: US National Institutes of Health (NIH) starts requiring grant applications to complete a new section describing efforts to authenticate antibodies.

Sep. 2016: International Working Group for Antibody Validation (IWGAV) formulates directives to evaluate antibodies, outlining five conceptual pillars for antibody validation (Genetic, Orthogonal, Independent, Expression of Tagged Proteins & Mass Spectrometry). Following the announcement, Thermo Fisher Scientific announces the creation of a comprehensive workflow to assess antibody specificity using immunoprecipitation combined with mass spectrometry (IP-MS).



EVOLUTION

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