



# 125 YEARS

## Antibody Discovery and Development

From early explorations of vaccination to present-day clinical trials, antibody-based research and therapies have long demonstrated their enormous potential to benefit human health.

This year we celebrate the 125th anniversary of the use of antibodies to treat diphtheria and tetanus and the advancement of the humoral theory of immunity. We encourage you to explore the rich history of antibodies and to share our passion for research supporting the next wave of innovations in this field.

**1971**  
ELISA assay developed independently by Eva Engvall and Peter Perlman (21)

**1972**  
FACS instrument developed and patented by Len Herzenberg's lab at Stanford University (22)

**1975**  
Georges Köhler and César Milstein develop hybridomas leading to the production of mAbs (23)

**1976**  
Susumu Tonegawa describes somatic recombination of immunoglobulin genes to account for incredible diversity (24)

**1978**  
Hybritech becomes the first mAb company (25)

**1979**  
First patent on hybridoma technology awarded to Wistar Institute (26)  
Western blotting, perhaps the most widely used immunoassay in research, is invented by Harry Towbin et al. (27)

**1960**  
Radioimmunoassay developed by Rosalyn Yalow and Solomon Berson (18)

**1965**  
Thomas Tomasi identifies secretory immunoglobulins (IgA) (19)  
First fluorescence based assay developed by Martin Fulwyler (20)

**1966**  
Kimishige Ishizaka et al. and S.G.O. Johansson & Hans Benich independently identified IgE as the reaginic antibody (reviewed in 7)

**1967**  
Kimishige Ishizaka identifies IgE as the reaginic antibody, binding the molecule that induced its synthesis (reviewed in 7)

**1953**  
Wallace Coulter awarded a patent on Coulter principle, enabling flow cytometry (12)

**1955**  
Niels Jerne proposes natural-selection theory of antibody formation (13)

**1956**  
Kappa and lambda light chains, then known as Bence Jones proteins, are shown to be two separate proteins by Leonard Kogrod and Rose Lipari (reviewed in 7)

**1957**  
Clonal selection theory proposed by Frank MacFarlane Burnet and David W. Talmage (14, 15)

**1959 and 1962**  
Different regions of antibody structures independently elucidated by Gerald Edelman and Rodney Porter (16, 17)

**1940**  
Karl Landsteiner and Alexander Weiner identify Rh antigens (8)

**1942**  
Albert Coons labels antibodies with FITC originating the field of immunofluorescence (9)

Jules Freund and Katherine McDermott demonstrate use of adjuvants to stimulate antibody production (10)

**1944**  
IgM is described independently by Jan Waldenström with Kai Pedersen as well as Henry Kunkel (reviewed in 7)

**1948**  
Astrid Fagraeus discovered antibody production in plasma B cells (11)

**1938**  
John Marrack proposes Antigen Antibody binding hypothesis (6)

**1939**  
Arne Tiselius and Elvin Kabat discover the first antibody isotype, gamma-globulin (reviewed in 7)

**1981**  
The lab of Herman Eisen develops the first anti-pTyr antibody (28)  
Hybritech delivers first mAb product to measure IgE in blood to diagnose allergic reactions (29)

**1982**  
Angus Nairn, et al. develop the first phospho-specific antibodies (30)

**1984**  
hCG antibodies used to develop 5 minute pregnancy test (31)

**1985**  
John Lis and David Gilmour develop Chromatin Immunoprecipitation (ChIP) assay (32)

**1986**  
Sean P. O'Neill and Joseph Wu awarded patent for quantitative immunoprecipitation assay (33)

**1980**

**1990**  
John McCafferty et al. report the use of phage display for antibody discovery (34)

**1995**  
Katherine Knight and colleagues at Loyola University, Chicago, USA published first paper on rabbit mAb development (35)

**1996**  
Prostascint<sup>®</sup>, radio-labeled anti-PSMA (prostate specific membrane antigen) imaging antibody approved by the FDA (36)

**1997**  
Idoc markets the world's first mAb treatment for lymphoma (Rituxan<sup>®</sup>) (37)

**1998**  
Herceptin<sup>®</sup> approved for breast cancer treatment (38)

**1999**  
CST established as an independent company and releases its first substrate motif antibody (#9611) (39)

**1890**  
Antibodies are shown to be active against diphtheria and tetanus, giving rise to a humoral theory of immunity (Emil von Behring and Kitasato Shibasaburo) (1)

**1891**  
Observed transferrable immunity (Emil von Behring and Kitasato Shibasaburo) (2)

**1896**  
Jules Bordet identifies complement as an antibacterial, heat-labile serum component (3)

**1890**

**1900**  
Paul Ehrlich develops antibody formation theory (4)

**1909**  
Almroth Wright publishes, "Studies on Immunisation", a collection of papers describing opsonization in the context of therapeutic immunization (5)

**1990**

**2000**  
Abgenix develops Xenomouse<sup>®</sup> which produces fully human antibodies (40)

**2004**  
Erbixub<sup>®</sup> approved by FDA for treatment of colorectal cancer (41)

**2006**  
CST released its first XP<sup>®</sup> antibody developed using the proprietary XMT<sup>®</sup> method (42)

**2000**

**2012**  
CST publishes NG-XMT<sup>™</sup> method, a proteomics approach to developing mAbs (43)

**2013**  
Kadcyla<sup>®</sup> (ado-trastuzumab emtansine), an antibody-drug conjugate, receives FDA approval as late-stage breast cancer treatment (44)

**2014**  
Yervoy<sup>®</sup> (ipilimumab), a monoclonal anti-CTLA4 antibody and the first immune checkpoint cancer therapy, receives FDA approval as a late-stage melanoma treatment (45)

**2010**

**2015**  
CST releases The CST Guide: Pathways & Protocols, a comprehensive scientific and technical resource for cell biology researchers (46)

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