

From activation induced cytidine deaminase (AID) to Casting and decoding model (C&D) in high affinity antibody generation

Chun Yang, M.D.

Abstract

It has been considered a major breakthrough on the discovery of activation induced cytidine deaminase (AID) in antibody generation with increased affinity in the past decade or so. Many scholars even claim that the AID mechanism detailed in the antibody diversity has solved the long mystery of somatic hypermutation (SHM), class switch recombination (CSR), and gene conversion (GC). Furthermore, the AID mechanism seems well explaining affinity maturation of antibody with the doctrine of random mutation, natural selection, and recombination. This implies that no new model is needed to develop. To my opinion, I certainly appreciate the discovery of AID in immune response. However, I think using AID mechanism to explain random mutation, natural selection, and recombination is not a complete and efficient mechanism as soon as the casting decoding model (C&D) is conceived in 2011 (Yang C. Casting and decoding model of protein RNA signal transduction in the affinity maturation of antibody, < www.energinity.com/2011proceedings1.pdf >. AID does not answer questions such as why there are two types of antibodies, high avidity (low affinity / high capacity, such as Ig M) and low avidity (high affinity / low capacity, such as Ig G). Why it is usually high avidity response first and then follows high affinity response. Also scholars often question how AID mechanism is actually recruited to a specific Ig locus, VDJ genes. AID also targets other non- Ig genes, where it can cause tumorigenic mutations and translocations. Only if the specificity issue of AID recognition of Ig genes is resolved then the mechanism of antibody diversity can be further accomplished. Casting and decoding model can answer at least three questions – the specific targeting Ig loci, the transition from high avidity to high affinity, and the high efficiency. Casting decoding model, as a prediction, can integrate the first response, the secondary response, antibody and antigen binding dynamic, immune memory, RNA sensor, VDJ gene recombination, AID, and quantitative biology etc. all currently available data. Casting and decoding model has apparent higher information energy efficiency (IEE) than AID that explains random mutation, natural selection, and recombination.

January 17, 2014