

SOT

In Vitro Lecture and
Luncheon

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Multicellular Model Systems for *In Vitro* Toxicity Testing—Strengths and Challenges

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In Vitro Co-Culture Biological Models

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Presentation Objectives

- Benefits and challenges of *in vitro* approaches in toxicology
- The 3 Rs in the welfare of animal use in research
- Two *in vitro* co-culture models for inducing B cells to become antibody secreting plasma cells
- The two model systems will set the stage for discussing cell:cell interactions and the impact on data interpretation

Why use *in vitro* approaches in toxicology?

The 3 Rs

- **Replace** the use of animals with alternative techniques, or avoid the use of animals altogether.
- **Reduce** the number of animals used to a minimum, obtain information from fewer animals or more information from the same number
- **Refine** the way experiments are carried out to make sure animals suffer as little as possible (i.e., improvements to procedures to minimize pain, improve animal welfare, better housing).

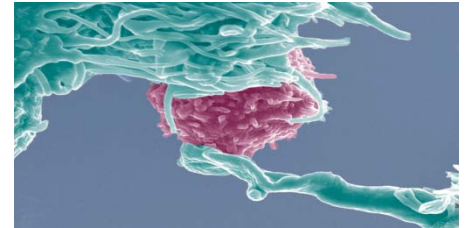
Elucidating the Underlying Mechanisms



Organismal



Organ



Cellular

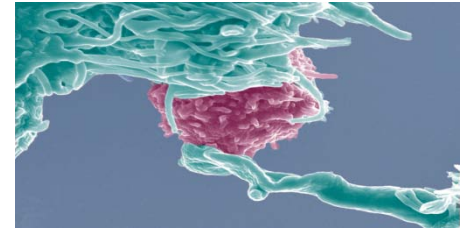
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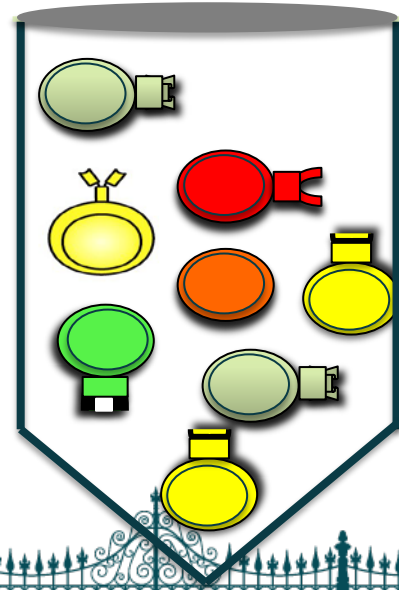


Cellular

Challenges with In Vitro Approaches



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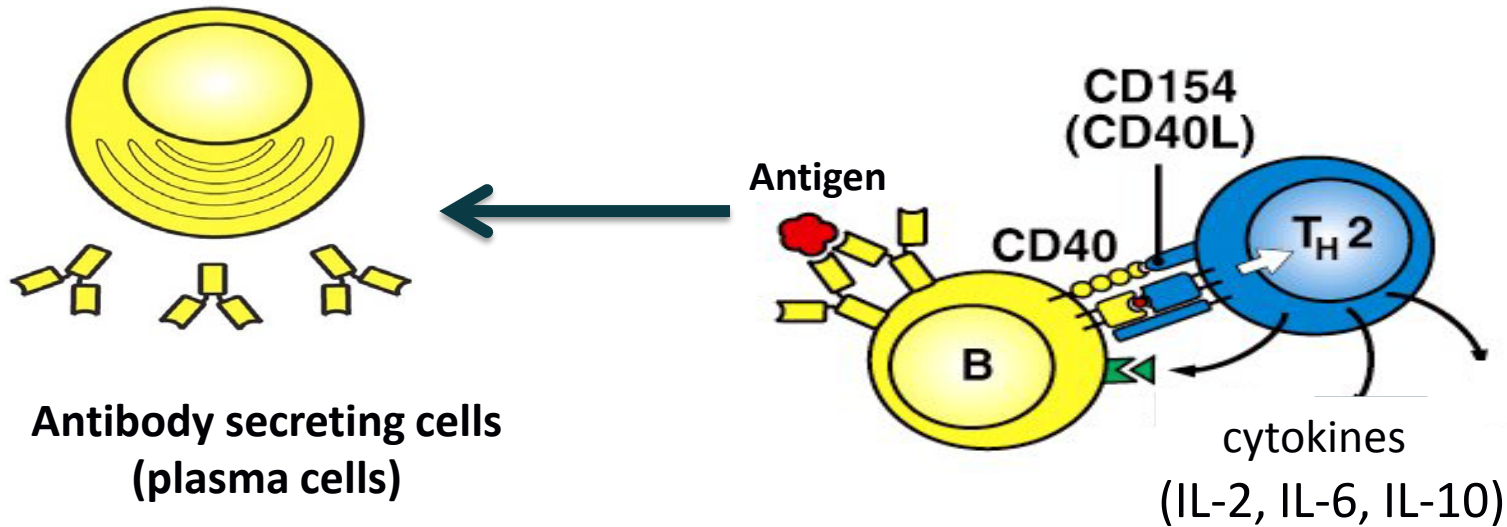
Example: Measurements of B Lymphocyte Function

Role of the B cell is to secrete antibody to protect the host against pathogens.

In vivo - Quantify circulating antibodies in blood directed against an antigen (e.g., vaccines such as tetanus or hepatitis).

In vitro - Quantify antibodies production or number of antibody producing cells using circulating B cells.

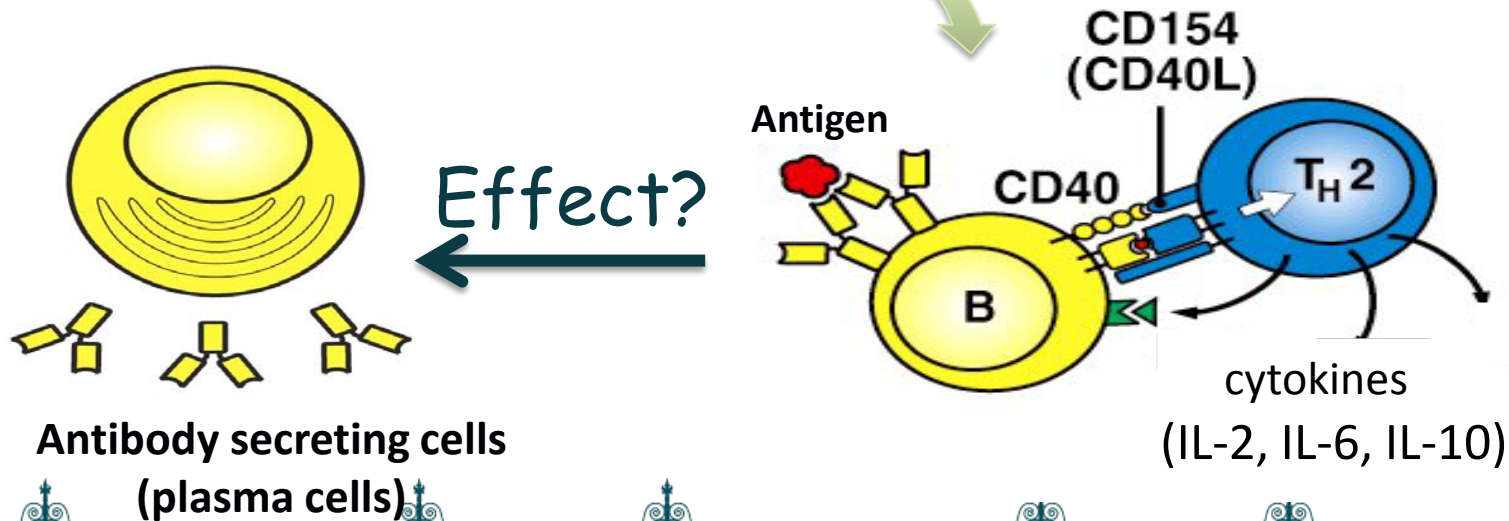
CD40-CD40L Interactions Provide a Crucial Signal for B cell Differentiation



(Modified from Janeway's Immunobiology)

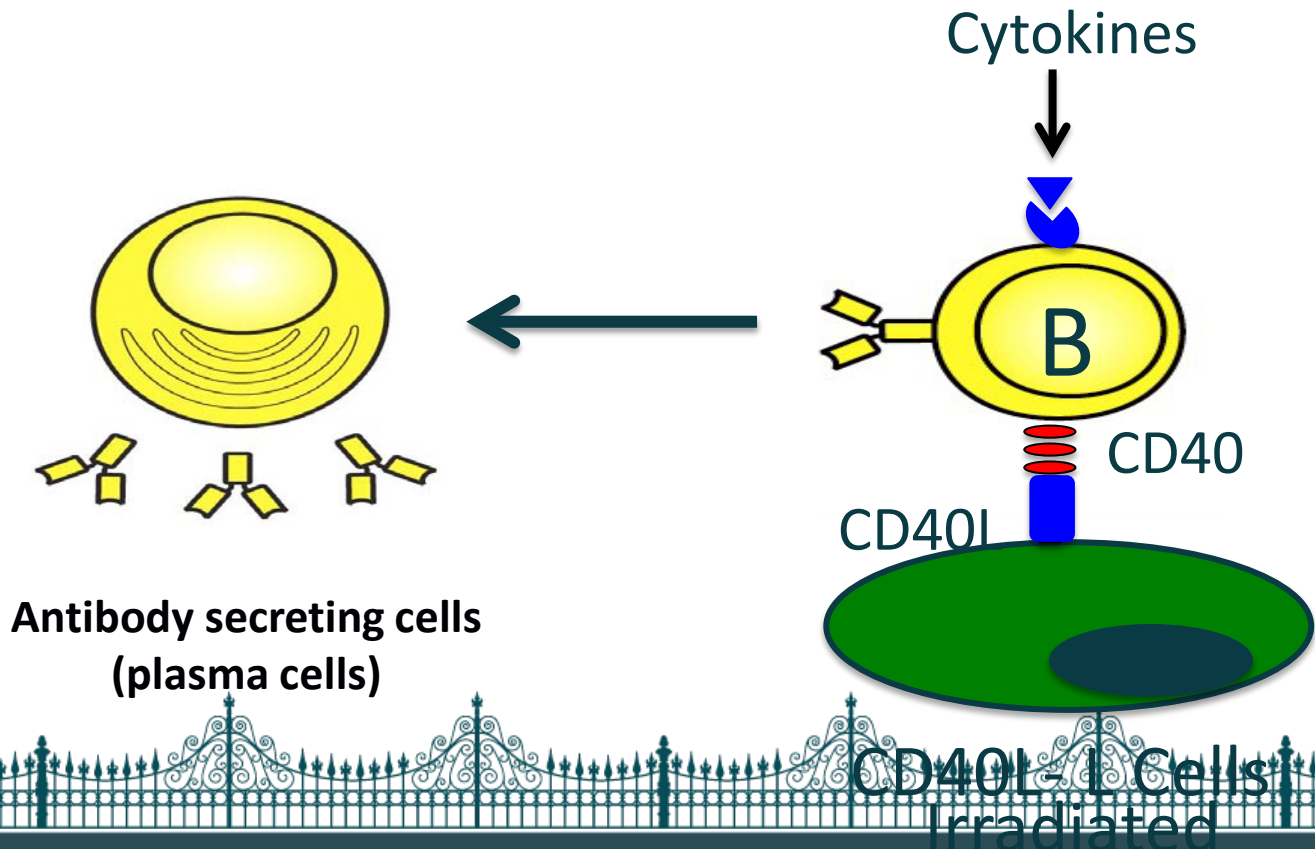
CD40-CD40L Interactions Provide a Crucial Signal for B cell Differentiation

Toxicant (TCDD)

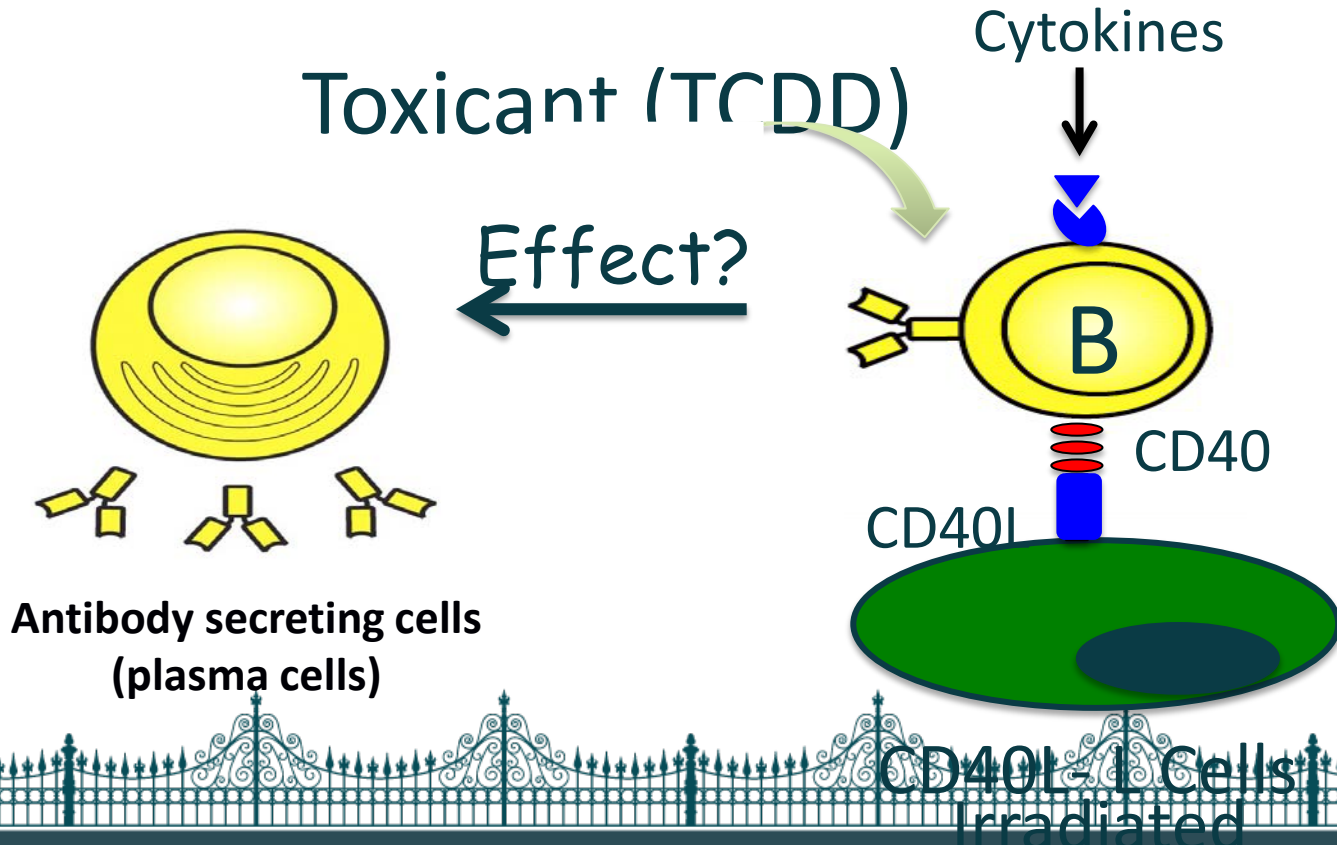


(Modified from Janeway's Immunobiology)

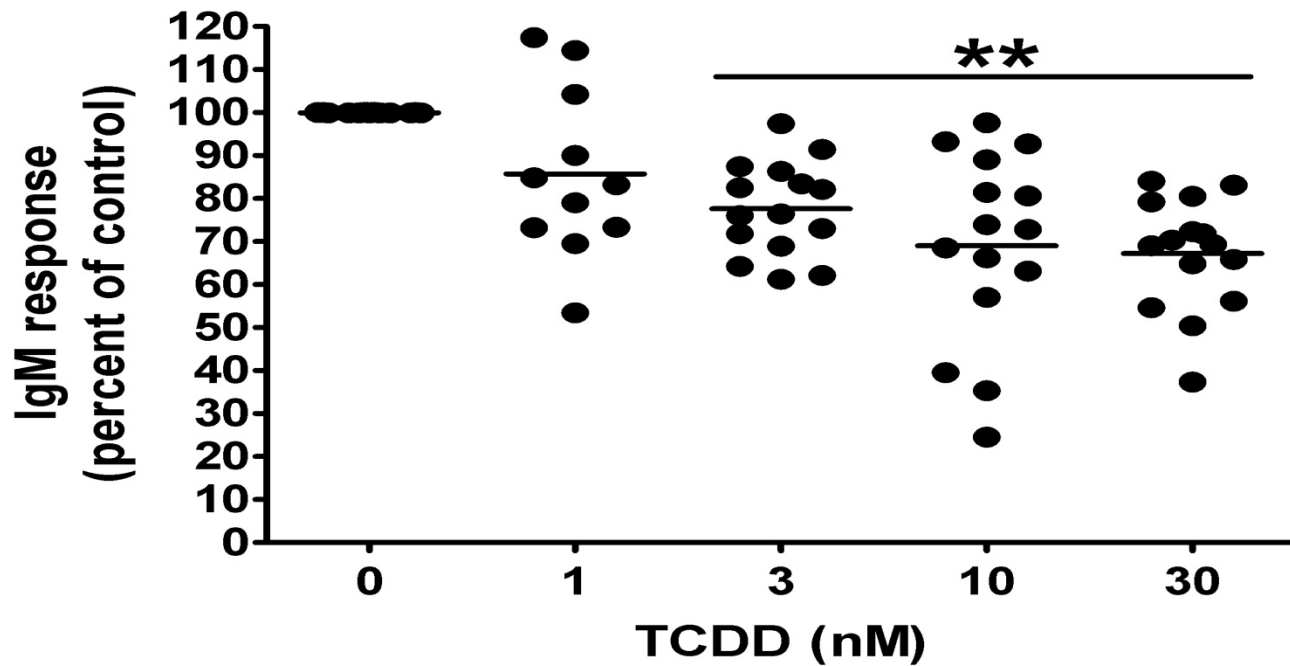
Surrogate CD40L-induced IgM Response



Surrogate CD40L-induced IgM Response



Suppression by TCDD of the CD40L-Induced IgM Response in Human Peripheral Blood B cells



Final Poll

