New Frontiers in Immunogenicity Research for Biosimilars in CDER

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Overview

- Immunogenicity overview
- Components of an immune response
- Immunogenicity risk assessment of biosimilars
- BSUFA III research related to immunogenicity

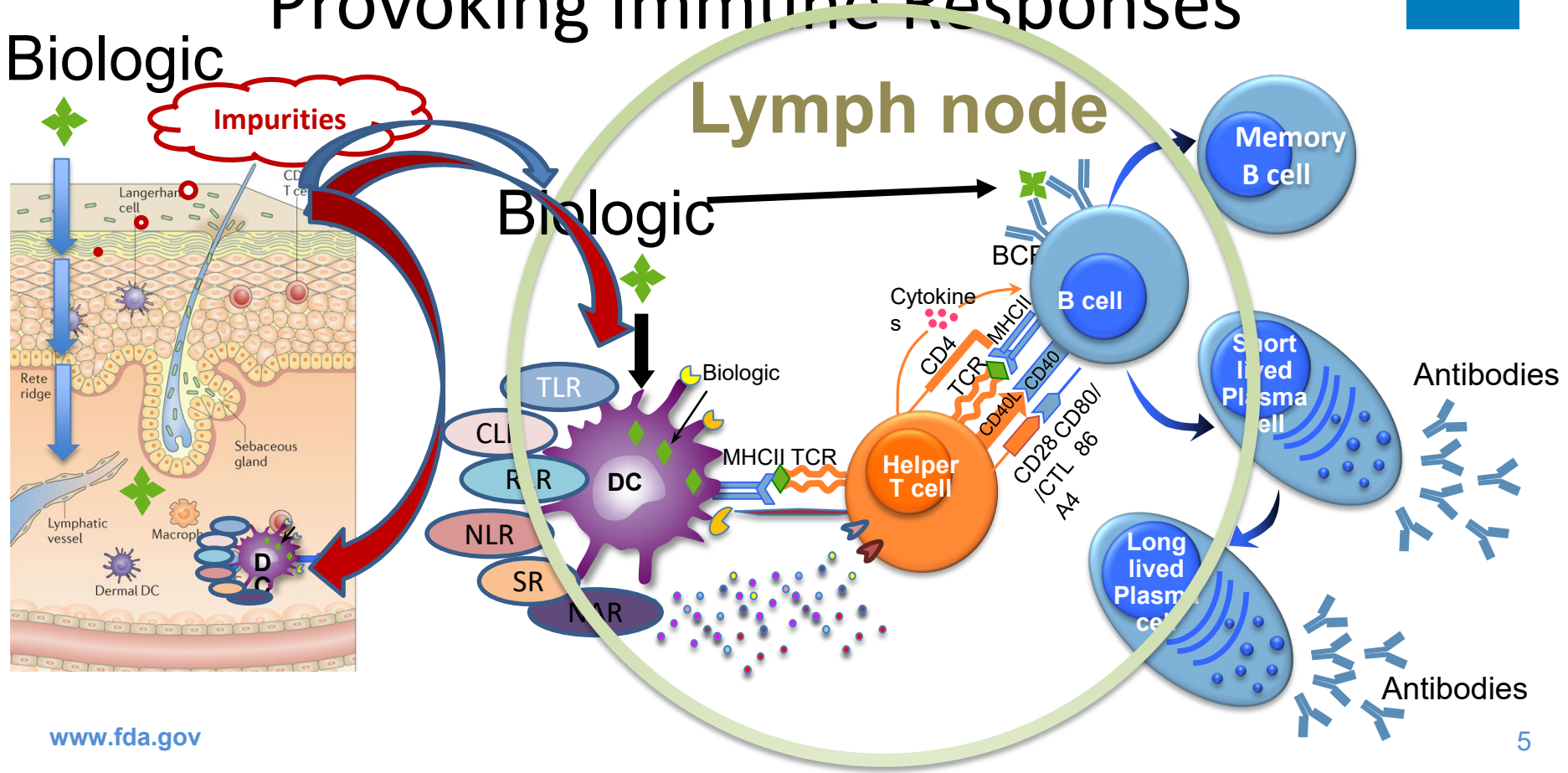
Immunogenicity

- The ability of a substance to provoke an immune response
- Immunogenicity of biologic products can result in:
  - Adverse events such as hypersensitivity reactions
  - Changes to pharmacokinetics, pharmacodynamics, efficacy
- Impact from immunogenicity frequently caused by anti-drug antibodies

Immunogenicity

- Immunogenicity is unwanted for therapeutic biologics
- Examples of the negative impact of anti-drug antibodies:
  - Pure Red Cell Aplasia in patients treated with epoetin
    - Anti-drug antibodies cross-reacted with patients' own EPO
  - Loss of efficacy in patients treated with adalimumab

APCs and Thelper Cells are Critical in Provoking Immune Responses



Immunogenicity Risk Assessment

- Factors that impact the risk of developing anti-drug antibodies (ADA)
  - Process related
  - Product related
  - Patient related
  - Disease related
  - Treatment related

Immunogenicity Risk for Biosimilars

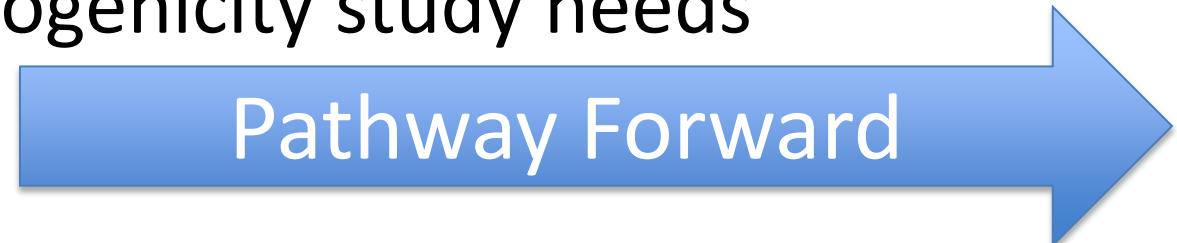
- Biosimilars are not required to match impurities
- Impurities can impact immunogenicity
- Uncertainty around immunogenicity risk from:
  - Process related impurities e.g., host cell proteins
  - Product related impurities and variants e.g., aggregates

Biosimilar Immunogenicity Studies

- Biosimilar development programs include clinical studies
- Clinical studies assess that the biosimilar is not more immunogenic than the innovator product
- Clinical studies compare anti-drug antibody responses

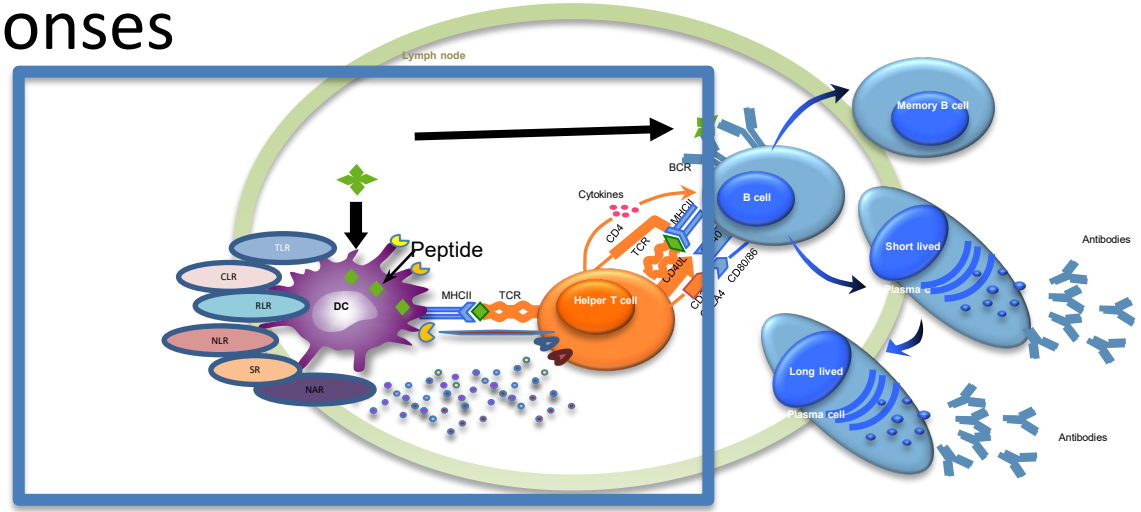
BSUFA Related Immunogenicity Research

- Reduce uncertainty about the impact of product and process related impurities
- Develop alternatives to clinical comparative immunogenicity studies
- Enhance risk frameworks for comparative immunogenicity study needs



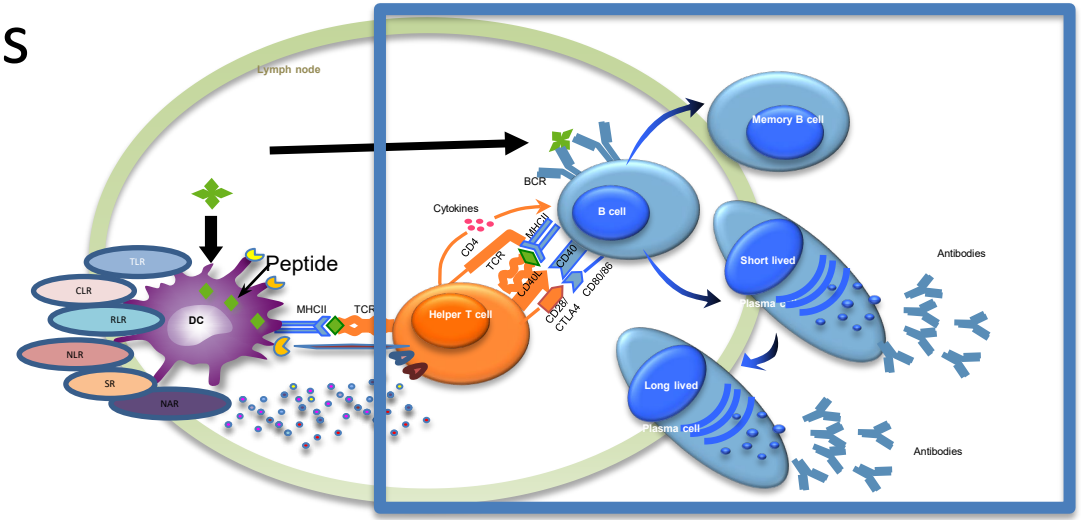
BSUFA Related Immunogenicity Research Goals

- Develop analytical methods for comparative studies
  - Evaluate for differences in initiating immune responses



BSUFA Related Immunogenicity Research Goals

- Develop non-clinical models for comparative studies
  - Evaluate for differences in generating immune responses



CDER Research Projects

- Validation of non-clinical immunogenicity models
- Production and optimization of humanized mice
- Develop acceptance parameters and standards for Innate Immune Response Modulating Impurities assays for biosimilars
- Address fundamental issues for in vitro immunogenicity testing

Summary

- CDER is developing and evaluating alternative approaches to clinical comparative immunogenicity studies
- Such alternative approaches will be important enhancements of risk-based approaches for comparative immunogenicity study needs

Summary

- Research is aimed at developing analytical methods and non-clinical models to be used as alternatives to clinical comparative immunogenicity studies

Next up:

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