

**Harvard Medical School Department of  
Continuing Education and the Renal Division  
of Brigham and Women's Hospital**



*Nephrology Rounds*  
May 2008

**T-Cell Costimulation Blockade: Immunoselective Maintenance  
Immunosuppression Versus Tolerance Induction in Transplantation**

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**Objectives:**

This issue of *Nephrology Rounds* will help the reader to develop an understanding of:

- the major families of costimulatory molecules and their role in allograft rejection and tolerance
- novel and emerging concepts in the field of costimulation, including the following:
  - discovery of novel positive and negative costimulatory pathways and their complex interactions
  - differential costimulatory signaling requirements among CD4+ and CD8+, as well as naïve, effector, and memory T cells
  - discovery of costimulatory ligands and the location of their expression
- reasons for failure of costimulation blockade strategies to induce tolerance in larger animals and humans.

**Questions:**

1. In addition to antigen recognition by T cells as presented by antigen-presenting cells (APCs), activation of T cells requires interactions among several other receptor-ligand pairs belonging to costimulatory pathways.

True

False

2. Costimulatory pathways can only transmit positive signals to T cells leading to their activation.

True

False

3. Some costimulatory ligands have recently been discovered in parenchymal tissues.

True

False

4. Cytotoxic T-lymphocyte antigen-4 (CTLA-4)/B7 and programmed death (PD)-1/PD-L pathways transmit positive costimulatory signals to T cells, leading to their activation and expansion.

True

False

5. The CD40-CD154 costimulatory pathway belongs to the CD28 superfamily of costimulatory molecules.

True

False

6. Both naïve CD8 T cells and memory T cells are less susceptible to inhibition by costimulatory blockade strategies and thus are major challenges to the induction of tolerance.

True

False

7. Anti-CD154 therapy was tested in a limited pilot study of renal transplant recipients, but the trial was halted after significant thromboembolic events developed.

True

False

8. LEA29Y (belatacept) is a new generation of CTLA4-immunoglobulin (Ig) that is 10-fold more potent in inhibiting T-cell activation *in vitro*.

True  False

9. LEA29Y was able to induce tolerance to allografts in primates.

True  False

10. LEA29Y is as effective as cyclosporine in preventing acute rejection at 6 months in renal transplant patients.

True  False

11. This issue of *Nephrology Rounds* adequately addressed the topic, and the data and discussion were fair and balanced.

AGREE  DISAGREE

12. Potential conflicts of interest disclosed by the author on the back page were properly expressed.

AGREE  DISAGREE

13. The information presented in this issue of *Nephrology Rounds* will increase my clinical knowledge and improve the care of my patients.

AGREE  DISAGREE

14. *Nephrology Rounds* from Brigham and Women's Hospital and Harvard Medical School is an effective CME program.

AGREE  DISAGREE

Comments/Topic Suggestions: \_\_\_\_\_

To receive AMA category 1 credit, you must correctly answer 60% of questions 1-10, and answer 11-14.

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