Addressing immune tolerance issues in inflammatory bowel disease and adeno-associated virus based gene transfer

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Propositions

1. A gene therapy approach for the local expression of therapeutic agents in the gut or a cell therapy approach using regulatory T cells or mesenchymal stromal cells may offer an alternative treatment for gastrointestinal inflammation (this thesis).
2. The major hurdle for successful re-administration of AAV vectors is the induction of neutralizing antibodies to capsid epitopes by the initial administration (this thesis).
3. Cross-administration of AAV serotypes 5 and 1 is an effective solution for repeated hepatic gene transfer (this thesis).
4. An attractive alternative to modulate immune responses against proteins delivered by AAV vectors is miRNA-based regulation of transgene expression (this thesis).
5. Depending upon the conditions, AAV is capable of priming immunity or inducing tolerance—both passively, through ignorance or anergy/deletion, as well as through active forms of suppression (Mays *et al., Mol Ther*, 2011; 19 (1): 16–27).
6. Studies in which AAV vectors were introduced to the systemic circulation of human subjects demonstrated that pre-existing humoral immunity to AAV vectors profoundly reduces the efficiency of transduction of a target tissue (Mingozzi *et al.*, *Gene Ther*, 2013; 20(4): 417–424).
7. It is becoming increasingly clear that the metabolic phenotype of DCs dictates their activation and immunogenicity. However, many of the details and underlying mechanisms of how cellular metabolism controls the functional properties of DCs remain to be determined (Everts *et al.*, *Front Immunol,* 2014; 5: 203).
8. Both *ex vivo* expansion with adoptive transfer and *in vivo* manipulation to expand and augment the function of endogenous Tregs represent promising strategies to treat autoimmune and alloimmune conditions (Singer *et al.*, *Front Immunol*, 2014; 5: 46).
9. The important thing is not to stop questioning. Curiosity has its own reason for existing (Einstein, from statement to William Miller, as quoted in LIFE magazine, 2 May 1955).
10. The oldest, shortest words— "yes" and "no"— are those which require the most thought (Pythagoras, As quoted in Numerology for Relationships: A Guide to Birth Numbers (2006) by Vera Kaikobad).
11. I am among those who think that science has great beauty (Maria Skłodowska-Curie, as quoted in Madame Curie: A Biography (1937) by Eve Curie Labouisse).
12. The responsibility of tolerance lies with those who have the wider vision (George Eliot, The Mill on the Floss, 1860).