Discussion Summary

Professor Anderson began with an overview of gene therapy research, outlining the number of current trials worldwide, where they are occurring, diseases treated, and vectors used. She then turned to ethical concerns raised by gene therapy clinical trials. A number of deaths, most prominently that of Jesse Gelsinger, revealed significant lapses of research integrity, among them, PIs with conflicts of interest, patients enrolled who failed to meet enrollment criteria, and lapses in informed consent. Despite concerns about patient safety and unintended mishaps, the assumption is that scientists will overcome these ethical and technical problems, with the result that we will eventually have gene therapies effective against a range of diseases and conditions.

The prospect of continued gene therapy trials led Prof. Anderson to ask what makes clinical trials in gene therapy go awry. Where, for example, were the voices of the nurse study coordinators and others responsible for patient safety? Why did they find themselves unheard in voicing ethical concerns? This question led to research into the operations and decisions that bear on gene therapy clinical trials, in particular the role of the study coordinator. Anderson presented the results of two pilot studies she conducted: the first a survey of the characteristics of study coordinators (education and certification, roles and responsibilities, ethics training); the second a series of in-depth interviews with ten nurse study coordinators and the clinical challenges they face.

A key factor in good clinical practice and ethical conduct, she found, was the relationship between the Principal Investigator (PI) and nurse study coordinator. Among concern were PIs too busy or not (regularly) on site, insufficiently trained in the biochemistry of the construct, inattentive to patient or family concerns, and committed to the protocol at the expense of patient safety. Despite these difficulties, study coordinators interviewed manifested a high level of protectiveness toward their PIs and the protocol.

Prof. Anderson next described her current project, an ethnographic study of multiple site gene therapy trials, for which she has just received NIH funding. The aim of this larger study is to describe the norms and practices of gene therapy research by understanding who the players are in each of the institutions involved (academic, regulatory, industry, clinical), the complex nature of the entire enterprise, and how it all functions. Results of this study are meant to draw attention to the need for best practice standards and education in all types of settings in which gene therapy is conducted. The hope is to enhance public trust in gene therapy research and perhaps promote patient participation.

In directing the group towards rethinking the cultural milieu of the research study, Prof. Anderson concluded by introducing two alternative ways to think about ethical decision making in this setting. She first compared the usual principle-based model of bioethics (applying principles of autonomy, beneficence and justice) to a model of “narrative ethics” — of
listening to the stories, or viewpoints, of all the participants (see this month’s readings). Anderson then also briefly described Margaret Urban Walker's notion of moral conversation in community (see readings assigned for this month). Both of these alternatives provide directions to explore in looking for more effective ways of establishing high ethical norms in the setting of gene therapy (and other) clinical trials.

Key points of discussion

- The difficulty of the role of study coordinator, particularly for nurses who are trained first and foremost to advocate for patient well-being. Nurses tend to see trial participants as patients first, subjects second.

- The possibility and/or desirability of separating the role of patient advocate and study coordinator.

- The underlying ethical issue of clinical trials enrolling very ill or dying patients who frequently “will do anything” to get well. Isn’t there something unethical about the very idea of clinical trials on vulnerable patients?

- The need for IRBs to establish exit points from gene therapy trials to allow participants, particularly very ill ones, on-going opportunity to evaluate their continued participation.

- The need for more training in gene therapy and clinical research for study coordinators (and PIs).

- What efforts are being made to license, credential, or otherwise certify nurse coordinators in gene therapy (and other) clinical trials? Is there a national or regional association working on certification standards?

- Insufficient training in clinical ethics and responsible conduct of research creates an atmosphere that makes it possible to ignore or justify “cutting corners,” human insensitivity, and bad science.

- Ethical issues in gene therapy (and perhaps clinical trails in general) are far broader and more basic than the issue of informed consent on which “we have pinned all our hopes” since the Belmont Report in the 1970s.

- The model of “narrative ethics” provides a useful alternative to the usual bioethics or ethical principles model. The narrative model allows for more sensitivity to conflicting values and priorities, moving away from abstract reasoning to a process aimed at creating the kind of cultural milieu in which all team members can exercise their moral voice.