

Enhancing research in regenerative medicine

The American Society of Hematology (ASH) convened a working group of experts from the fields of hematopoietic stem cell biology, embryonic stem cells, transplantation biology, and gene therapy at the urging of the Committee on Government Affairs with the goal of developing a “white paper” to inform recommendations to ASH and appropriate parties at the National Institutes of Health (NIH) about the need for additional research in the area of regenerative medicine. The focus of the workshop was specifically to contribute to an ongoing dialogue about the potential use of a variety of stem/progenitor cells and their cell products in treating human diseases. The workshop focused on 4 major topics: (1) identifying questions that need to be answered in the broad area of regenerative medicine; (2) determining where gaps exist in research in this area; (3) pinpointing the windows of opportunity in investigation of this topic; and (4) establishing a list of priorities that may form the basis for future federal grant opportunities.

Recommendations to the NIH

1. To recognize the field of regenerative medicine across the interests of multiple NIH institutions. The field can thus be considered a paradigm of the NIH Roadmap with an emphasis on novel funding mechanisms and inter-Institute cooperation and collaboration.

2. To review and improve current funding mechanisms from NIH in regenerative medicine to ensure that resources adequately meet the needs of basic discovery, translational, and clinical applications of this evolving technology. Suggestions for improvement include:

- a. P01/R01 grants reviewed by a “Regenerative Medicine Translational Review Panel/Study Section” that includes broad expertise in basic and clinical investigations and realization that Good Manufacturing Process (GMP) development and validation are critical to the field, but difficult to fund in the usual NIH Study Section format.

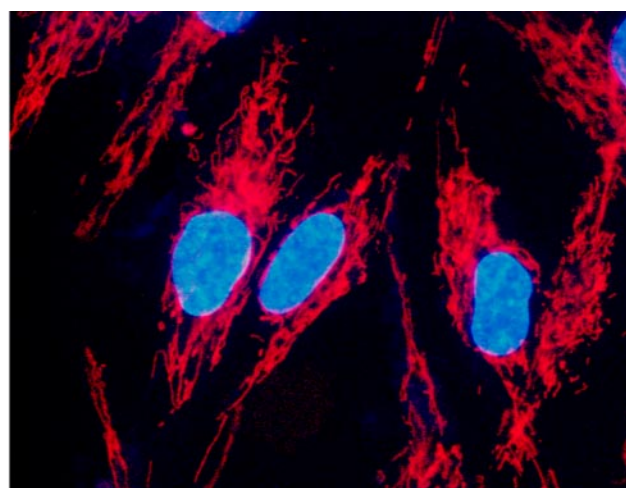
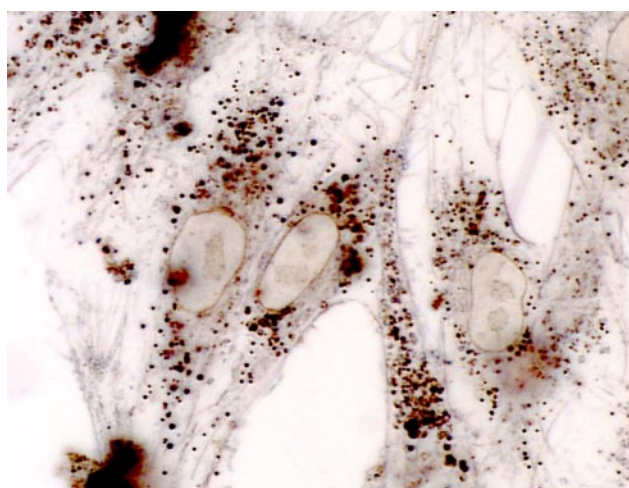
- b. To encourage additional pharmaceutical/biotechnology partnerships and collaborative grants.
 - c. To develop Requests For Application (RFAs) that focus on studying both the potential efficacy and the safety of these therapies, including patient-specific database registries for effectively tracking outcomes and adverse events of subjects receiving cellular reagents.
3. The NIH Office of Director should take the lead in establishing a regenerative medicine program or center at the NIH to facilitate resource utilization and coordination of NIH activities in this area.

Recommendations to the general scientific community

1. To foster improved communications between basic and clinical scientists in regenerative medicine.

2. To build a consensus for the design of clinical trials across multiple disease disciplines that optimizes the opportunity for data collection and dissemination. The guiding principles for such a consensus to address would include:

- a. To ensure adequate characterization of the cellular product to be used in human trials.
 - b. To have a defined long-term follow-up plan for all trials utilizing stem cell derivative products.
 - c. To bank a portion of all cell products infused into humans, or at a minimum, DNA from donor samples for future interrogation as the field progresses with both successes and failures.
3. To re-examine the current clinical trials methodologies and determine whether these designs are useful in the setting of cellular therapies.
4. To develop a consensus around the utility of animals and animal models to test efficacy and safety of cellular products.



Mesenchymal stromal cells (MSCs) show promise in tissue regeneration. The cells are highly metabolically active as shown by the high numbers of mitochondria (red; right panel) and interact closely with each other as shown in the unstained live cell preparation (left panel).

The online version of this article contains a data supplement.

Recommendations to ASH

1. ASH should take advantage of its strong convening power to foster both education and collaboration across all disciplines involved in the use of stem/progenitor cell products. Specific areas should be:

- a. Meet with the leadership of other relevant societies and organizations* to leverage multiple efforts where overlap in goals exists.
- b. Develop a consensus statement on the methodologies to be used to assess postinfusion efficacy and safety that are widely applicable across multiple diseases.
- c. Develop a consensus on general release criteria for cells.

2. ASH should encourage members with expertise to assist in the development of publications and educational materials on the topic of regenerative medicine, particularly on the use of stem cell derivatives. These materials should cover both technical aspects of the field and perspectives on (i) stem cell tourism; (ii) safety; (iii) the role of iPS cells and embryonic stem (ES) cell derivatives in hematologic diseases, particularly related to marrow failure and marrow failure syndromes; (iv) the role of adult stem/progenitor cells in tissue regeneration and their possible modes of action; and should be written for both scientific and lay audiences.

3. ASH should consider establishing an ad hoc scientific committee on regenerative medicine, including aspects of hematology in which the use of stem cell derivatives would likely initially occur at the clinical level. This ad hoc committee should include a focus on diseases such as bone marrow failure for which cellular transplantation is already in therapeutic use.

4. ASH should consider adding a session on regenerative medicine at its annual meeting. Examples of such possible sessions include a Tuesday afternoon special session; specific workshops on the use of adult stem/progenitor, ES, and iPS cells and other cellular products; a session on regenerative medicine in the Educational Program.

5. ASH should leverage the expertise and experience of society members in hematopoietic stem cell transplantation biology to establish hematologists as “opinion leaders” in the field. Through its marketing efforts, ASH should facilitate the use of these opinion leaders by not-for-profit disease groups and the lay press.

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*Professional and Scientific Organizations: AABB, ACC, AHA, ASBMT, ASN, CIBMTR, EBMT, EHA, FACT, ISCT, ISEH, ISSCR, NETCORD, NMDP, JACIE.

Patient Advocacy Organizations: LLS, ACS.