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Cytocompatibility evaluation of cell delivery devices using clinically relevant cells under exaggerated use conditions

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Abstract

The impact of medical device design on the delivery of cell-based therapies requires further investigation. Among the impacts to consider is that cells, or certain subsets of the therapy population, passing through devices may adhere to device materials and be lost from treatment (1). Cells may also encounter residual trace amounts of manufacturing agents that could induce apoptosis or push cells down an undesired differentiation pathway (1). To detect these potential failure modes, a panel of in vitro tests was developed to assess delivery device compatibility with clinically relevant cell therapies, which we define as device cytocompatibility.

Introduction

Blood and blood products are used in front-line treatments for patients with anemia, acute blood loss, metabolic disorders, and myeloablative procedures. More specific treatments using umbilical cord blood and bone marrow-derived concentrates are being evaluated in clinical studies. Human umbilical cord blood (HUCB) and bone marrow (BM) concentrate are composed of hematopoietic stem cells, neutrophils, platelets, and red blood cells (2). Therefore, HUCB (3-5) and BM concentrate were determined to be appropriate cellular models to evaluate device cytocompatibility. Parameters of cytocompatibility investigated include:

1. Cell recovery: Ensure that cells do not adhere to the device in an appreciable amount such that they compromise the intended dose for therapy.
2. Cell viability: Ensure cells are intact and not entering apoptosis following delivery through the device.
3. Cell proliferation: Ensure that replication competent cells are capable of dividing following delivery through the device.

Select cell delivery devices, primarily needle or catheter-based, were evaluated for cytocompatibility by characterizing cell recovery, cell viability, and cell proliferation following direct contact with the devices as compared to cells not exposed to devices. Cell contact time with the devices was under clinical use (a few seconds per the IFU) or exaggerated conditions (2 hours).

Objectives

To develop a battery of tests to verify the cytocompatibility of cell delivery devices using clinically relevant cell type(s) and to evaluate if these tests would be useful for design verification or lot qualification of devices.

Methods

Figure 1. Cell delivery devices, accessories, and cell processing supplies tested for cytocompatibility.

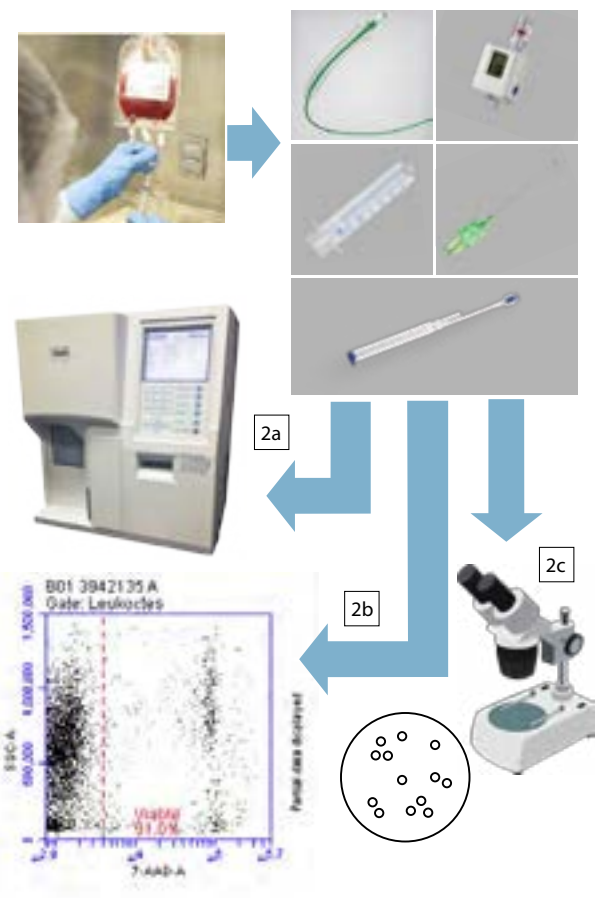

Figure 2. Cytocompatibility test methods: 2a) Cell recovery test. Cord blood or bone marrow was exposed to the cell contacting surfaces of the delivery device under clinical use (a few seconds) or exaggerated conditions (2 hours). Cell recovery was then determined using a Sysmex® hematology analyzer to count the number of nucleated cells recovered; 2b) Cell viability test. Cord blood or bone marrow was exposed to the delivery device per IFU or exaggerated conditions. Cell viability was then determined via flow cytometry (7-AAD); 2c) Cell proliferation test. Cord blood or bone marrow was exposed to the delivery device per IFU or exaggerated conditions. Cell proliferation was then determined via a colony forming unit (CFU) assay.

Results

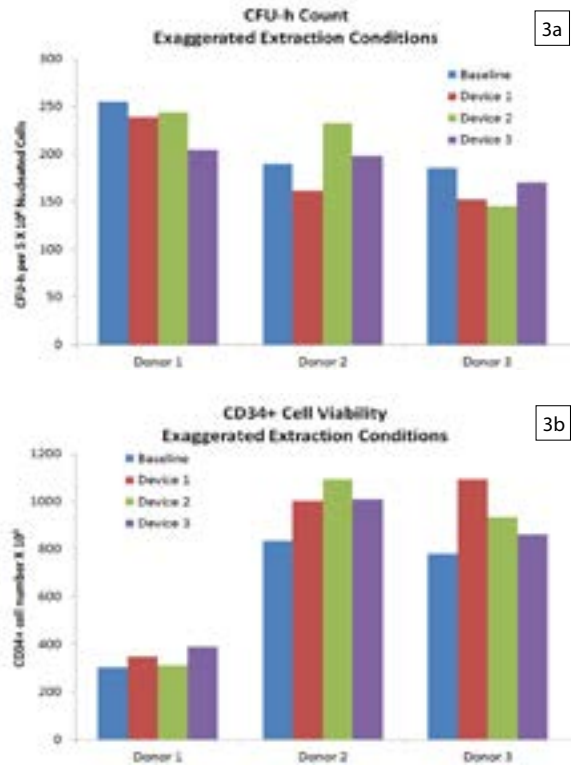

Figure 3: Proliferation and viability of BM cells after exaggerated exposure: 3a) Cell proliferation measured by CFU assay; 3b) Cell viability of CD34+ cells measured by flow cytometry.

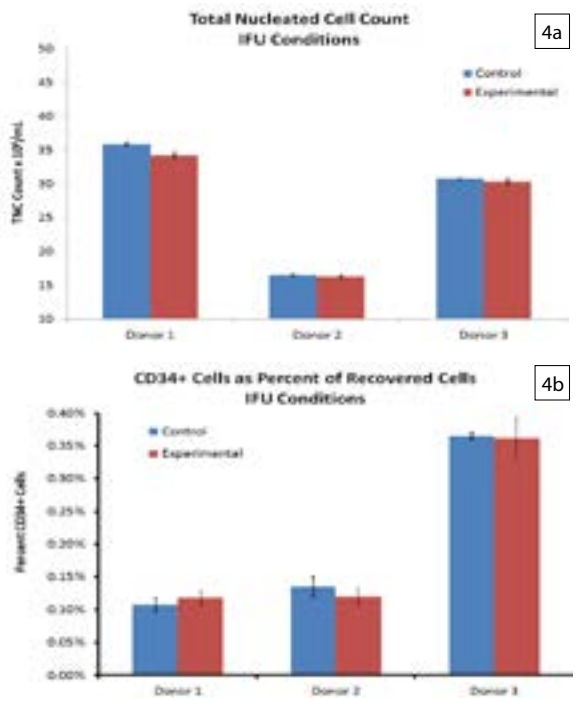

Figure 4: HUCB Cell recovery: (4a) Relative count of nucleated cells recovered after passing through device compared to control sample recovery; (4b) CD34+ cell recovery as a percentage of total leukocyte recovery (CD45+).

Results

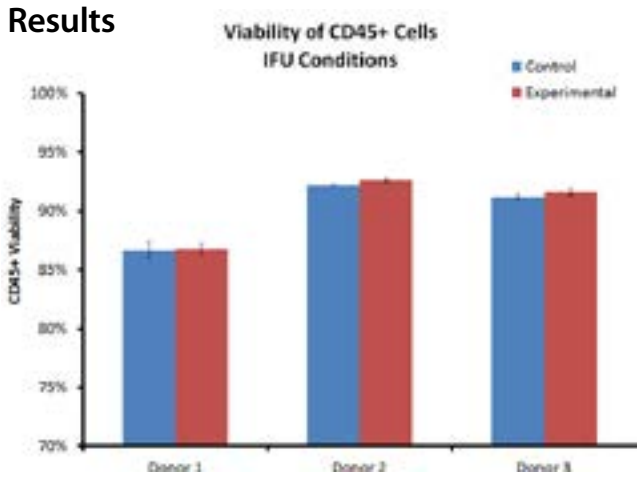

Figure 5: HUCB cell viability. Percent of viable cells recovered after passing through the test device relative to control sample viability.

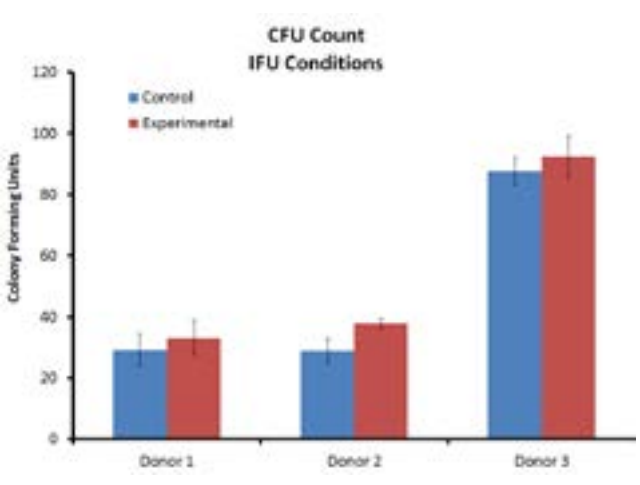

Figure 6: Proliferation of HUCB cells after exposure to device per IFU compared to control sample proliferation. Proliferation measured by CFU.

Conclusions

- Tests using clinically relevant human cell lines were developed to assess cytocompatibility for a wide variety of cell delivery devices.
- The effects of exaggerated contact with different devices on recovery, viability, activity, and proliferation of BM and HUCB were assessed.
- Results were influenced by the source of BM and HUCB.
- Cytocompatibility testing may be used as part of design verification or for device lot qualification.
- Manufacturing method, processing aides, materials, device and component-level design may influence cytocompatibility results.

References

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