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Date: Wednesday, May 29, 2024 at 6:06 PM
To: Claudette Mandac <cmandac@cirm.ca.gov>
Cc: Claudette Mandac <cmandac@cirm.ca.gov>
Subject: [EXT] Fw: CIRM bullet points

Hi Claudette,
I plan to attend the ICOC meeting tomorrow and present a shortened version of these bullet points. I hope this presentation can be copied to the committee.

- Within blood forming tissues, we showed that pure HSCs, only 1 in 100,000 bone marrow cells, are the only self-renewing cells,and that with this property they are the only longterm engrafting cells to rapidly regenerate vital blood cells.

- In the 1990s we treated women with metastatic breast cancer [MBC] with hi dose bone marrow ablative chemo, then rescued their blood formation with their own pure HSC—which we showed lacked cancer contamination—or mobilized blood [MPB], usually cancer contaminated. The median survival of MPB rescued women was 2 years, while with HSC was 10 years. By 15 years all MPB rescued patients were dead or had breast cancer, while of the HSC rescued women, 33% were alive without cancer[and are at over 25 years]. The companies that bought this technology did not even try to repeat the study.

- We also showed that MPB or CD34 selected grafts contained sufficient numbers of T cells to cause often lethal immune damage[called GvH] in genetically distinct recipients, still the greatest cost measure of BMT, while purified HSC –lacking T cells—cause NO GvH.
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- People with genetic blood diseases such as sickle cell anemia have two HSC avenues for cures. The first is to try to replace disease genes in human HSC by gene editing, but no company or group purifies HSC, and so for the past 30 years this hardly works and is expensive. The process is more efficient starting with HSCs. The second is our method to isolate pure HSC from healthy donors ,which do not cause GvH. Isolating pure HSC as in this grant for transplantation is rapidly curative, and much cheaper.

- We have also shown that transplanted pure HSC induce immunological tolerance of organ grafts from the HSC donor, eliminating the need for lifelong immunosuppression. We and others are differentiating HSC and other tissue stem cells from embryonic stem cells, a longterm and major CIRM goal.
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- We have subsidized $5-10M of our own donated money to provide the HSC sorting antibodies, and have signed contractual arrangements with Novartis and Stanford to supply antiCD34 and antiCD90 antibodies for free or at cost at Stanford, and potentially the CIRM alpha stem cell clinics. We claim no ownership or ip for these donations.
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- We have donated and will donate 2-4 new cell sorters to Stanford alpha Stem Cell LCGM to hasten this progress.

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- Our studies in the 1990s compelled us to find a way to use HSC as the platform for all CIRM regenerative medicine, and compelled me to co-author Props 71 and 14. Sadly, the initial science advisors ruled out this broad HSC discovery platform for CIRM funding.

  Irv Weissman