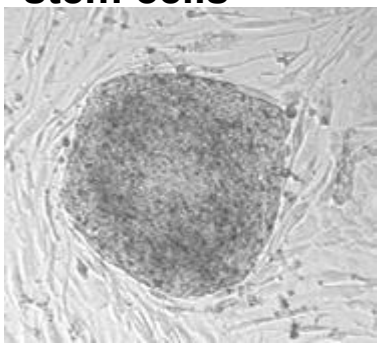
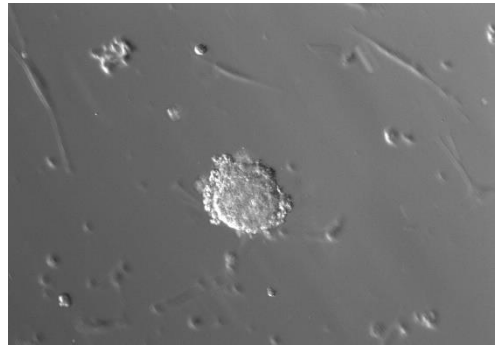
1. What's new?: (a) We have successfully cultured very early blood-forming "blast" cells from the "Presidential" H1 and H9 hESC lines

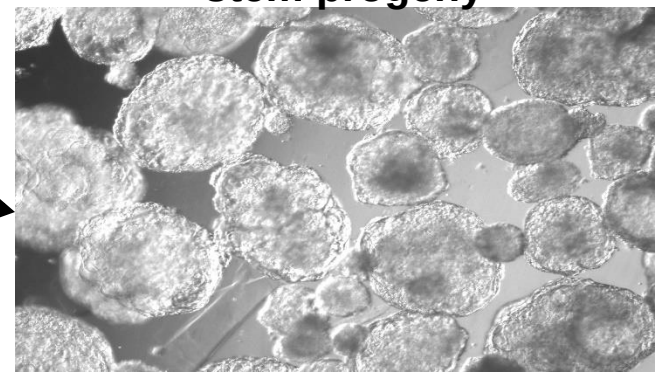
Colony of undifferentiated human embryonic stem cells



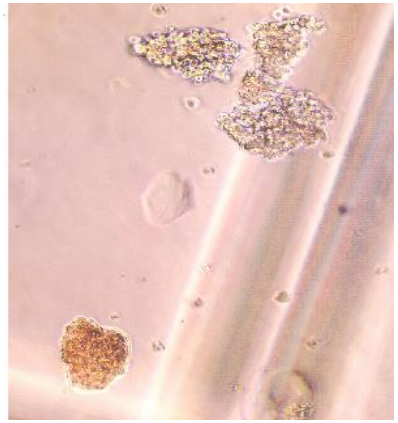
Day 2: Differentiating human embryonic stem cells

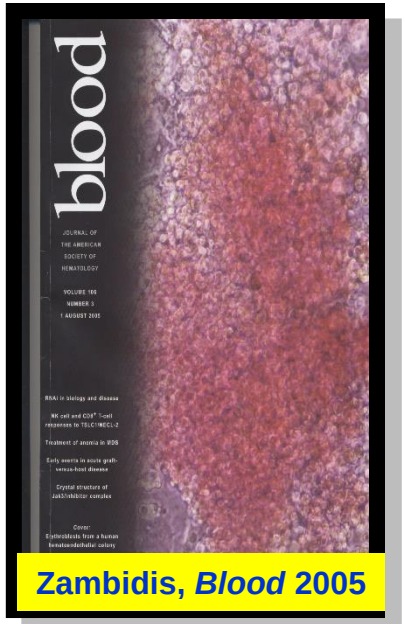


1-2 weeks later: Many differentiating human embryonic stem progeny

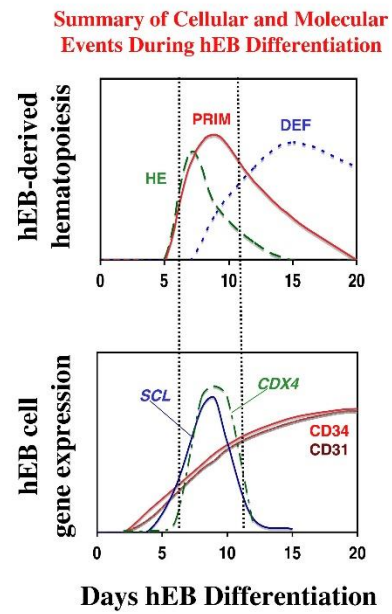


2 weeks later still: Colonies of functional blood cells

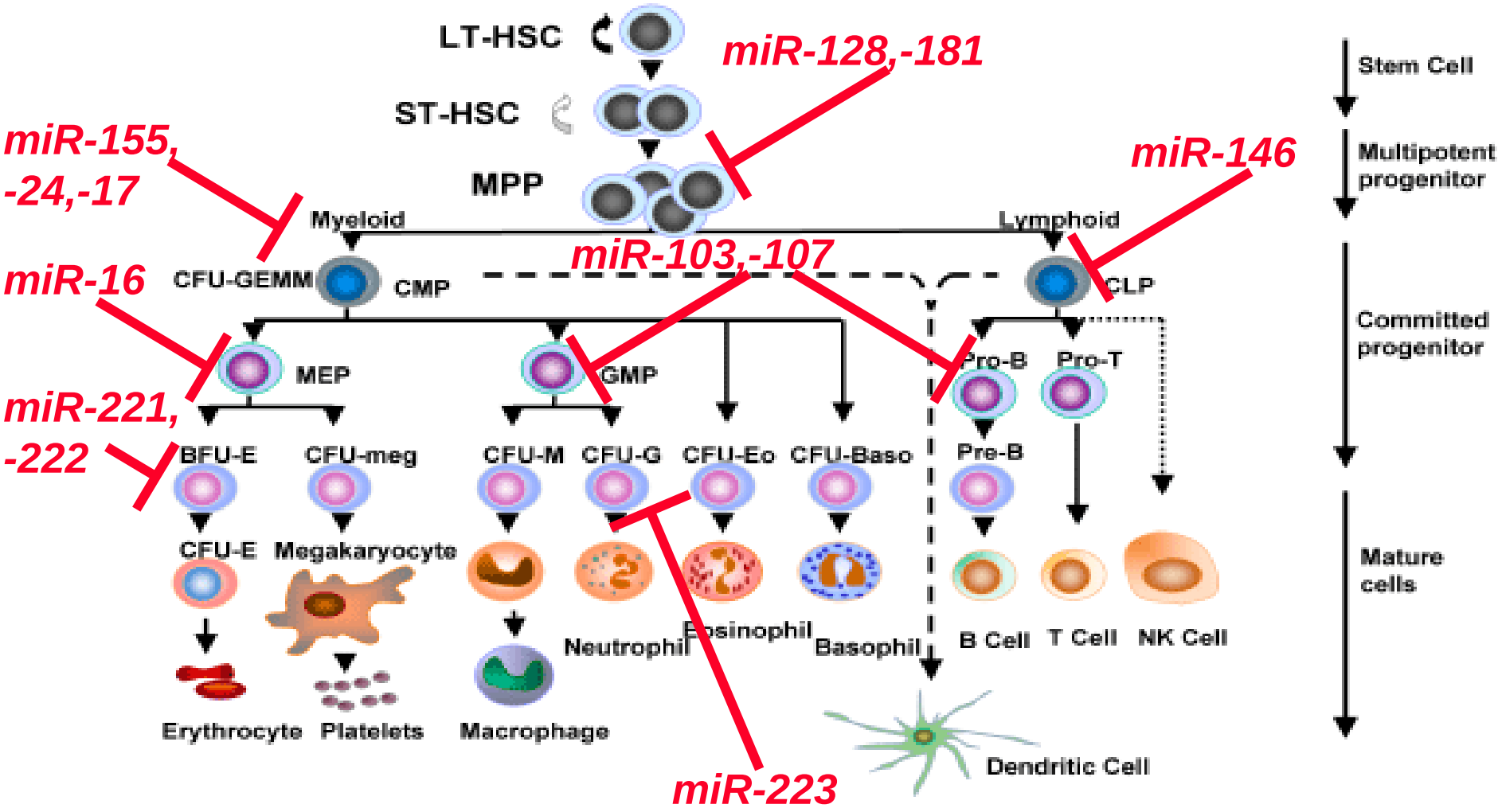




Zambidis, *Blood* 2005



2. What's new?: (b) We have discovered a new set of controlling molecules ("microRNAs") which restrain the growth and development of blood-forming stem cells



Georgantas, *PNAS* 2007

2. What slows our studies?

- **Old tools for embryonic stem cell research:**
  - **We can use only "version 1.0" ("Presidential") human embryonic stem cells (no antibiotics, slow growth, clinically limiting)**
- **Insufficient funding for embryonic stem cell research:**
  - **Slow development of preliminary data → delays in grant funding**
- **Strange barrier to scientific interactions:**
  - **Prohibitions prevent from federally-funded researcher from teaming up to bring in ideas and expertise, as we usually do in our open culture of discovery and translational science**

3. What is the promise of our studies?

- **Matching hematopoietic stem cell transplants (BMT) available for everyone**

- **Hematopoietic stem cell transplants to prevent rejection of transplanted organs, such as kidney, pancreas, etc (or hESC-derived organ-forming cells)**

- **Undertanding that will lead to new medicines to treat and prevent diseases (Whole-world treatments and preventions instead of expensive, first-world transplants)**

Why do I use embryonic stem cells in current studies of blood cell development?

- Embryonic stem cells can self-renew in the lab for years, and make enough hematopoietic stem cells to transplant many individuals (Hem stem cell transplant as a means to tolerize patients for transplants of stem cells to form organs such as kidney, pancreas, etc)
- Using embryonic stem cells, we can investigate very early steps in blood (and leukemia) development that occur even before a woman could know she was pregnant
- Embryonic stem cells can form a variety of cell types beyond blood
- Embryonic stem cells as models to understand cancer stem cells

Cancers likely originate in stem cells

➢ **Their longevity and (self-)renewal capacity should make stem(-progenitor) cells susceptible to the acquisition of both initiating and secondary oncogenic mutations (in the same cell):**

- ❖ Stem(-progenitor) cells persist long enough to accumulate the multiple oncogenic hits necessary for cancer development
- ❖ Stem(-progenitor) cells are already programmed to generate huge clones of identical or similar progeny cells

➢ **These cancer stem cells persist and maintain the fully-evolved cancers**

➢ **Are cancer stem cells vulnerable to inhibition of canonical stem cell signaling?**