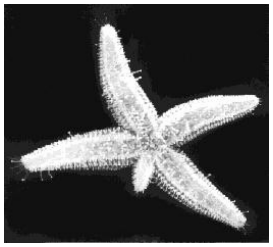
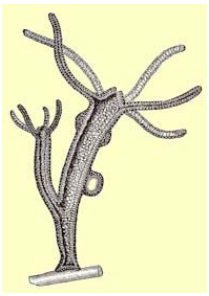
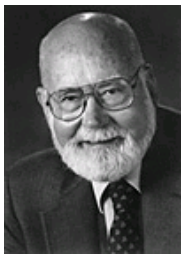
The History of Stem Cells – Selected Excerpts



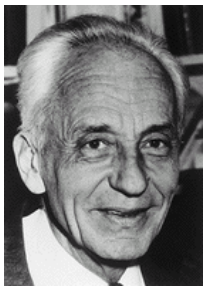
Among fishermen in Maine there is an old joke about the rookie fisherman who was so irritated at dredging up starfish from his oyster bed that he began chopping them up and flinging them over the sides of his boat in the hopes of eventually eradicating them. Unfortunately, as he later discovered, starfish have the remarkable ability to regenerate an entirely new starfish from a single part. Each one of the pieces he returned to the sea becomes another starfish. Tales (or tails) of tissue regeneration (as opposed to replacement) appeared as long ago as Aristotle. How they can perform such an act of reproduction was, amazingly, ignored for the 2,000 years that elapsed from the time of Aristotle to France of the 1600s





In Thomas' seminal paper (E.D. Thomas et al., *N Engl J Med* 257:491 (1957)), he showed that dogs could be protected against lethal doses of irradiation by intravenous injection of bone marrow cells. That, in turn led him to develop standardized methods for the collection and infusion of human hematopoietic (from blood) stem cells. These were, of course, derived from the bone marrow.

Like all revolutions, the emergence of a defined and therapeutic stem cell started with something startlingly off-kilter. A tumor with teeth. A cancerous tumor so disorganized that it had neurons, muscle, limb buds, hair follicles, a complex gut and, yes, teeth buds. A gumbo of differentiated stem cells that established, for the researcher studying it, the existence of a type of cell plastic enough to become any or all of these differentiated tissues.



In 1958, French medical researcher Jean Dausset made a critical discovery that defined all subsequent therapeutic cell research. Professor Dausset, then head of the Immuno-haematology Laboratory at the National Blood Transfusion Centre of France, described for the first time human histocompatibility antigens.

It was the work by Professor Georges Mathé, distinguished French oncologist and immunologist from Group Hospital Paul Brousse, which finally showed that living cells from a bone marrow graft could engraft and have therapeutic effect in an adult patient.

Dr. Arnold Caplan of Case Western Reserve University's oncology unit in Cleveland, Ohio, also duplicated Dr. Friedenstein's famous studies but then took them several steps further.

Catherine Verfaillie's lab at the University of Minnesota was studying mesenchymal stem cells about ten years ago when her graduate student at the time, Morayma Reyes, decided to omit cow serum from a culture of these bone marrow-derived stem cells. The cells prospered, dividing for several months. When Verfaillie and Reyes checked on their culture, they found that the cells had differentiated into endothelial cells, which are found on the inside of blood vessels.

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