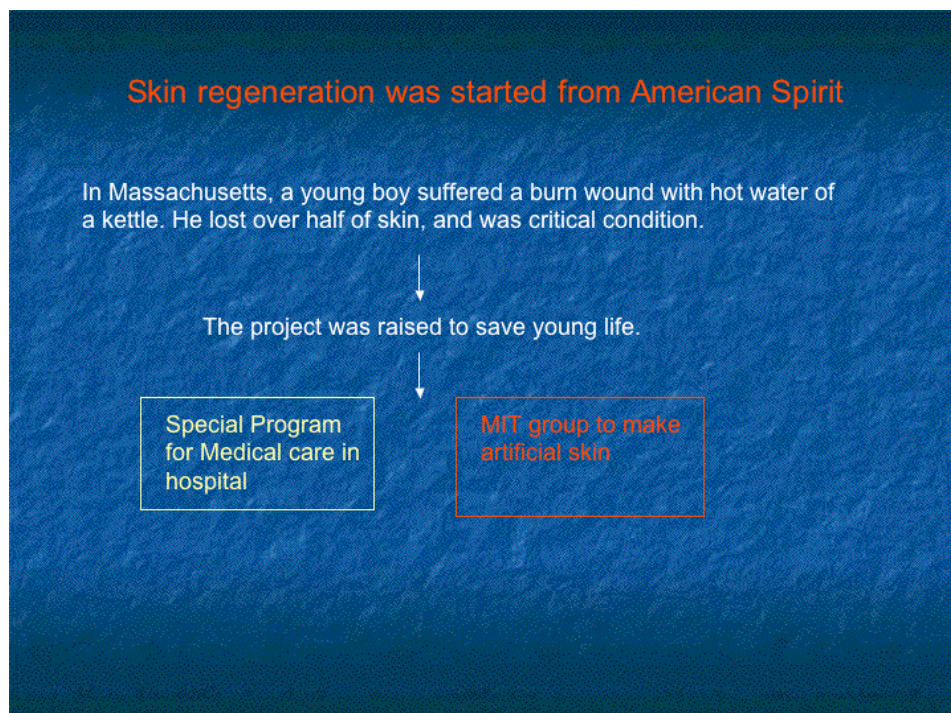


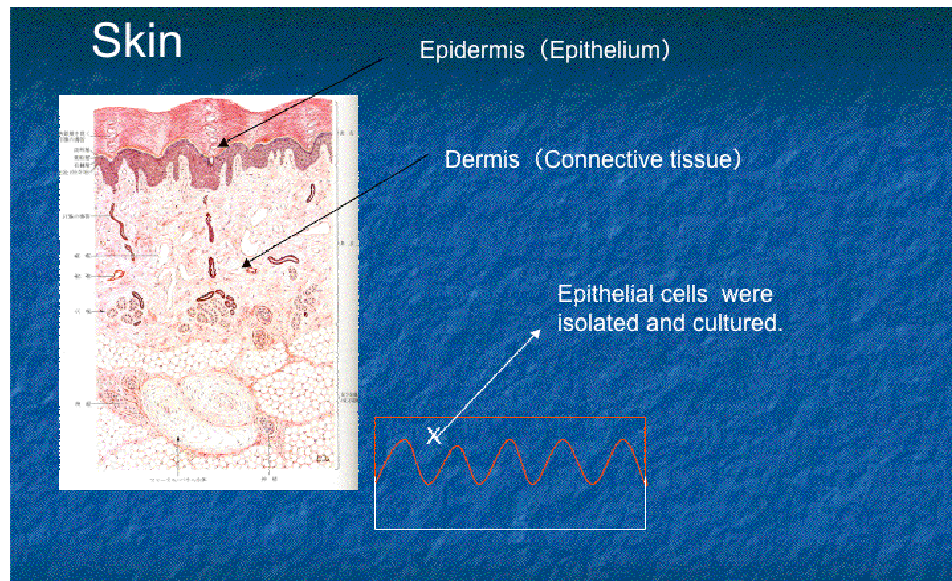
At this time, I would like to talk about skin regeneration. A study of skin regeneration started from American Spirit.



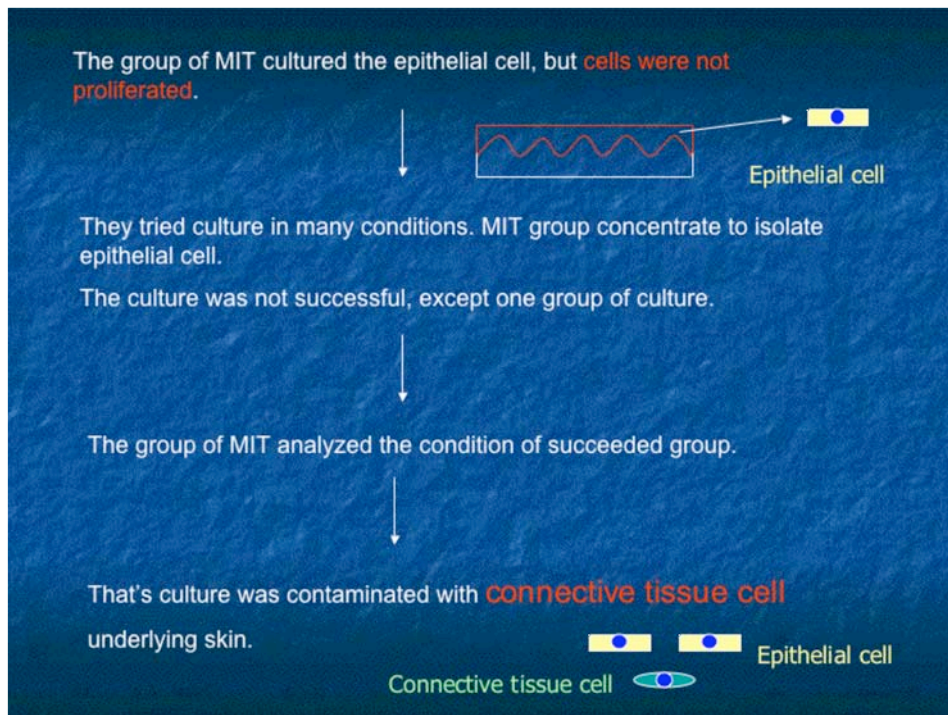
In 1970 in Massachusetts, a young boy was burned and he lost over half of his skin. At this time, American Spirit was raised. One is from hospital. One is from an MIT Group to make artificial skin. Dr. Green wanted to make artificial skin.



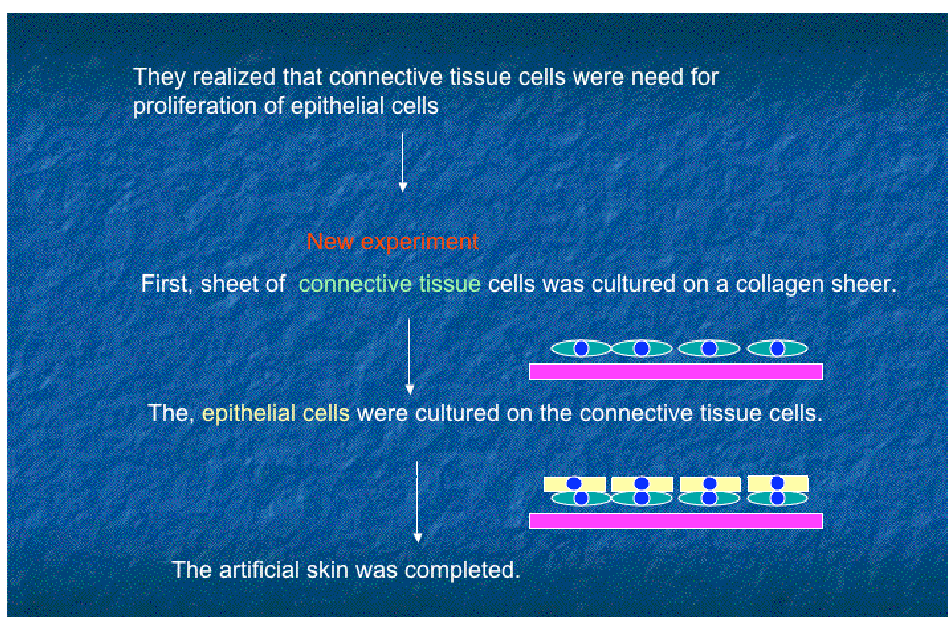
I would like to introduce the structure of the skin. Skin consists of two kinds of tissue. One is connective tissue called the dermis. The second is epithelium, which is called epidermis. These two kinds of tissues are connected. This is the skin.



A group at MIT started to isolate epithelial cells to make artificial skin. They wanted to collect and grow epithelial cells to make artificial skin. They tried to culture using many different but the cultures were not successful, except one group. Dr. Green analyzed everything and he found that the only successful group was contaminated with connective tissue. This fact became very important.



Dr. Green realized for the growth of epithelial cells, cells needed the help of connective tissue. That is the most important point. He started the experiment again. What he did was to first make a sheet of collagen and isolated the connective tissue and collagen. Then he used x-ray radiation to stop the proliferation of connective tissue. After that he cultured epithelial cells onto the connective tissue cells.



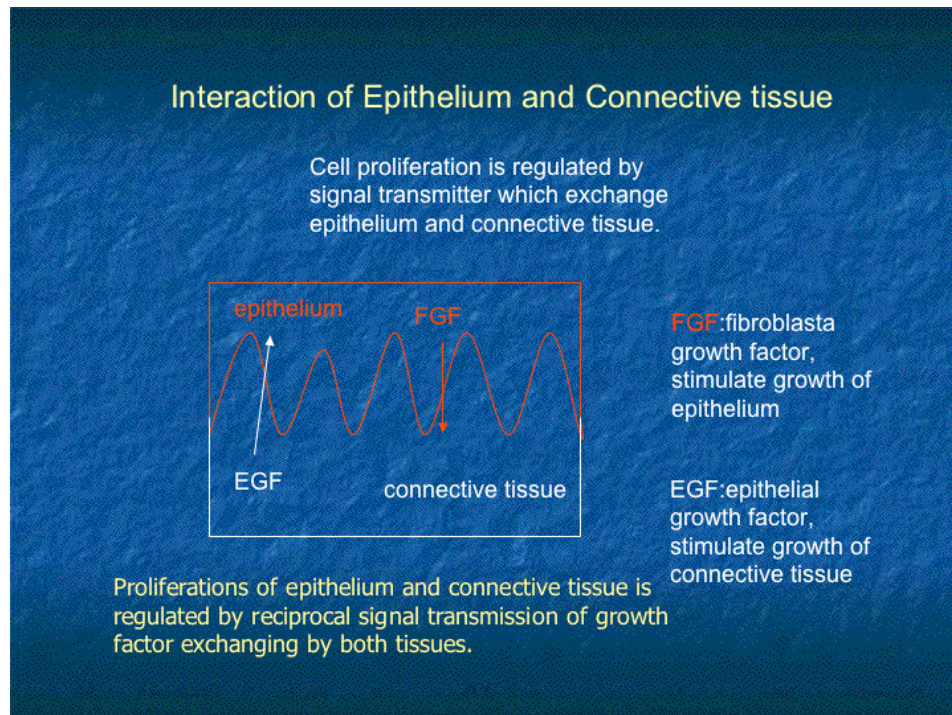
These are the conclusions of Dr. Green. Dr. Green concluded that connective tissue is needed for the growth of epithelial cells. He also concluded that he needed to co-culture with 2 types of different cells. This was the first work for tissue regeneration. The very important point is that connective tissue is necessary for the growth of epithelial cells.

**The group of MIT has demonstrated  
many evidences.**

1. Connective cell need for growth of epithelial cell.
2. Co-culture with 2 types of different cells
3. First work for tissue regeneration.

**“Connective cell is necessary for  
growth of epithelial cell.”**

Connective tissue cells stimulate growth of epithelia cells, and epithelia cells stimulate connective tissue cells.



Microphone dies. 5:49

Also, there's an increased number of leukocyte and blood platelets. The fibrogenesis nanoHAP is stronger than collagen. But the growth of epithelial is all the same. An important thing is the formation of accessory organ of skin. So collagen shows better results than nanoHAP. This is very important for us. If epithelia is to recover it has to be helped. Accessory organs refer to hair, sweat gland and subateous gland. Without this accessory organ, you get problems with dry skin, so morphogenesis is most important.

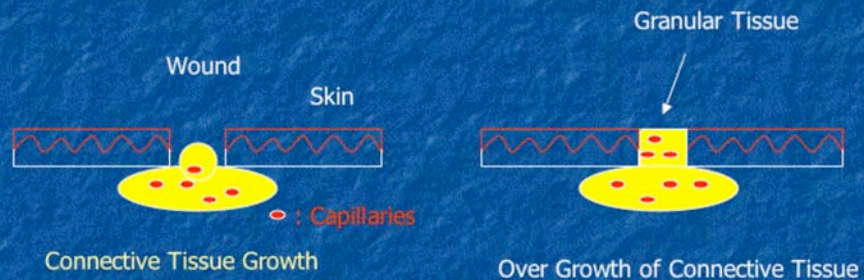
Result of Skin Regeneration

Time	Parameter	Collagen	Collagen	nanoHAP	nanoHAP	Skin defect
1d	Bleeding	+	++	+	+	++
1d	Leukocyte	+++++	++	+++++	++	+
1d	Blood platelet	+++++	+	+++++	+	+
3d	Fibrogenesis	++++	+	+++++	+	+
1d	Blood vessel	+++++	+	+++++	+	+
1d	Epithelial growth	+	+	+	+	+
5d	Epithelial growth	+++++	+	+++++	+	±
1d	Accessory organ of skin	+	+	+	+	±
7d	Epithelial growth	+++++	+	+++++	+	±
1d	Accessory organ of skin	+++++	+	++	+	±
10d	Epithelial growth	++	+	+	+	±
1d	Accessory organ of skin	++++	+	++	++	+

We have one problem in skin regeneration. It's caused by over growth of connective tissue. Sometimes, overgrowth leaves connective tissue exposed on the skin surface.

A problem in Skin Regeneration

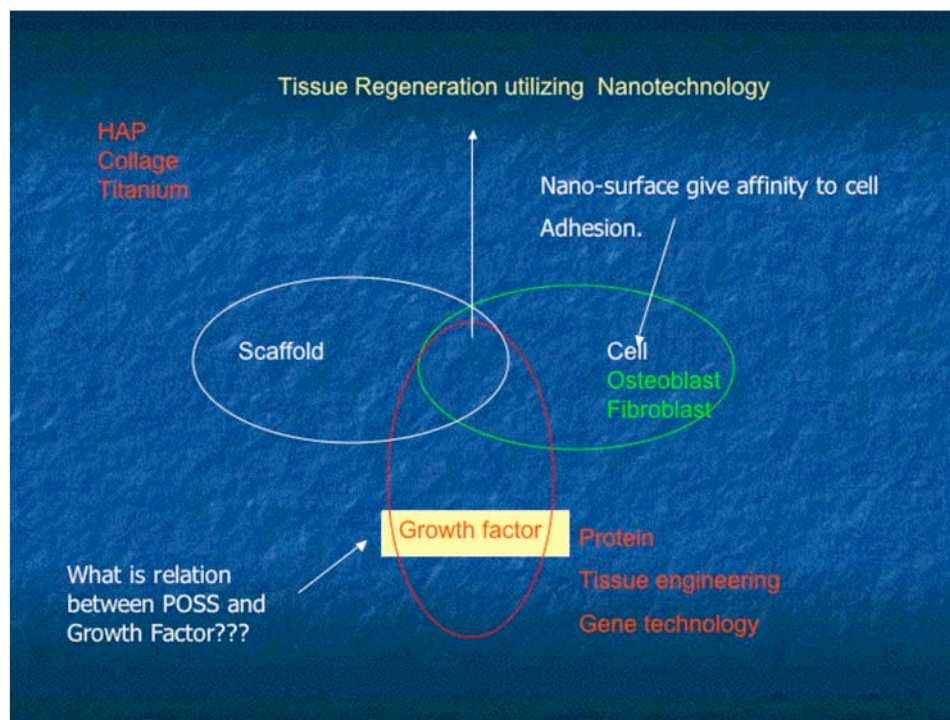
Granular Tissue Formation



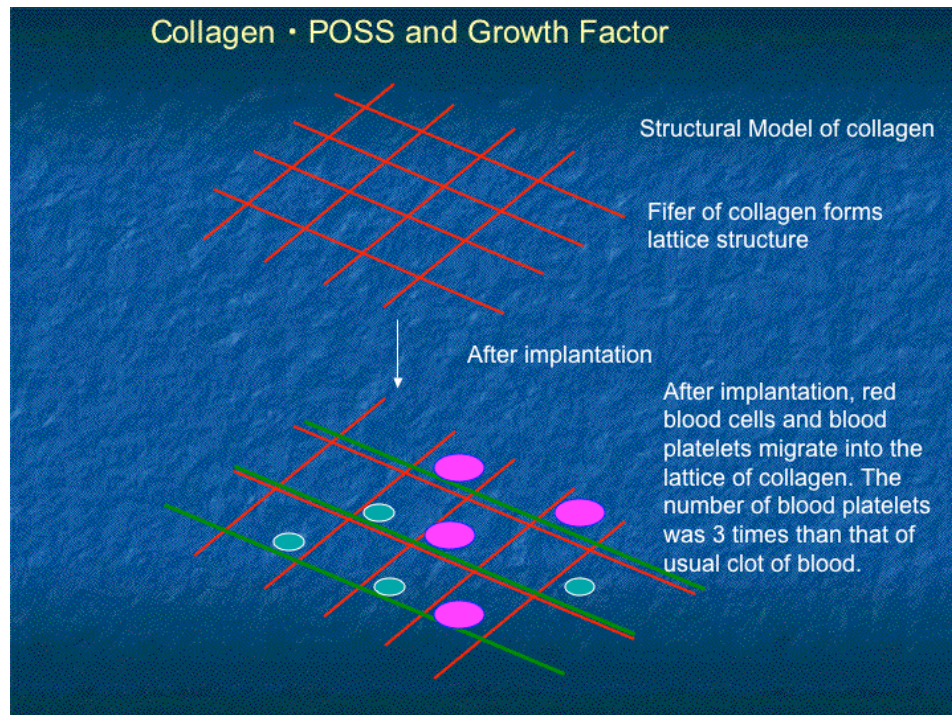
POSS does not stimulates over growth of fibroblasts, but stimulates differentiation of fibroblasts.

This is abnormal healing because from the outside, if you look at the face or skin, the skin color will look wrong. This is abnormal healing, but POSS<sup>®</sup> does help with these kinds of things because POSS<sup>®</sup> stimulates the differentiation of fibroblasts, but it doesn't effect their proliferation.

This is a matrix for tissue regeneration utilizing nanotechnology. There are three factors needed for skin regeneration. Scaffold, cells and growth factor. The question is how can POSS<sup>®</sup> stimulate growth factor? I would like to explain how POSS<sup>®</sup> effects the growth factor.

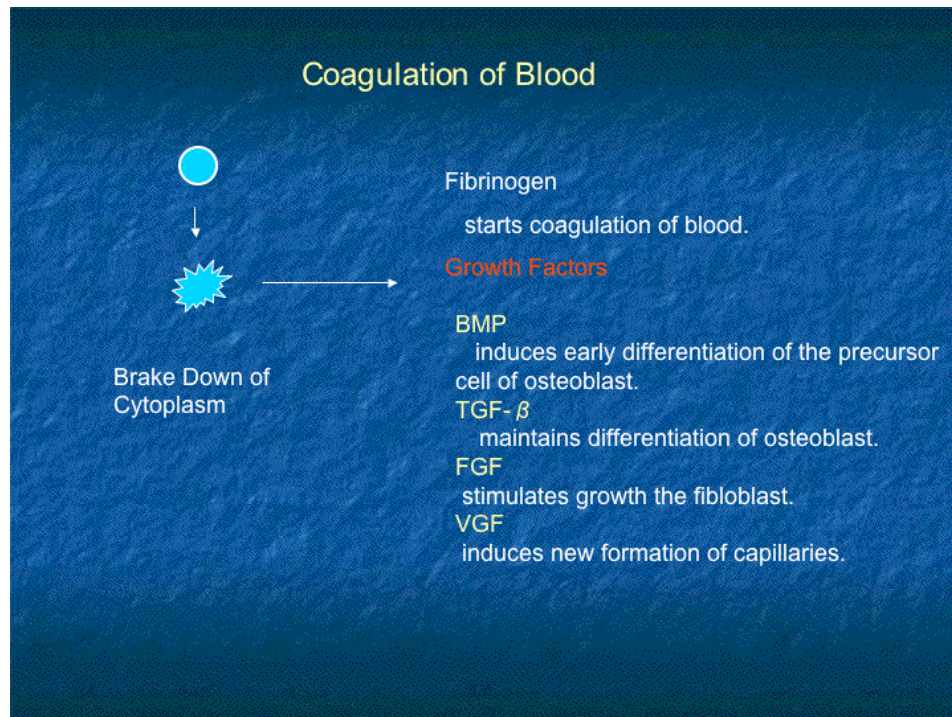


This is a model of collagen. Collagen is arranged like a lattice structure. After implantation, red blood cells and blood platelets migrate into the lattice of collagen. POSS<sup>®</sup> has a strong cell affinity to the blood cells, especially blood platelets and leukocytes.



I need to tell about the functional blood platelets. Blood platelets come from megakaryocytes in the bone marrow.

Once bleeding occurs, blood platelets come out from the capillaries and then there is a break-down of cytoplasm. When cytoplasm breaks down, blood platelets release many things. One is to promote coagulation of blood. The other one is growth factors. BMP induces early differentiation of the precursor cells of osteoblasts and fibroblasts. TGF- $\beta$  maintains the differentiation of osteoblasts and fibroblasts. FGF stimulates the growth of fibroblasts. VEGF induces formation of new capillaries.



These are the most important things. I studied coagulation with POSS<sup>®</sup> under normal conditions. With POSS<sup>®</sup>, I found three times the number of blood platelets. This is the reason POSS<sup>®</sup> works on the growth factor.

Using this philosophy, growth factor and scaffold and cells, we can prepare many things in the medical field. With titanium, we can make artificial joints and dental implants. For tissue regeneration, we can produce bone, skin, muscle and cartilage. This is a possibility but I think I can do it. Scaffolds for tissue engineering and genetic engineering. Even in tissue engineering, we need a scaffold. POSS<sup>®</sup> can be helpful with tissue engineering and genetic engineering.

## Application of BIO-POSS

### Titanium

hip joint, dental implant *etc.*

### Tissue regeneration

bone (fracture, osteoporosis)

skin

muscle

cartilage

### Scaffold for

tissue engineering

genetic engineering

Thank you very much.



