First in Man Synthetic Nanofiber Trachea

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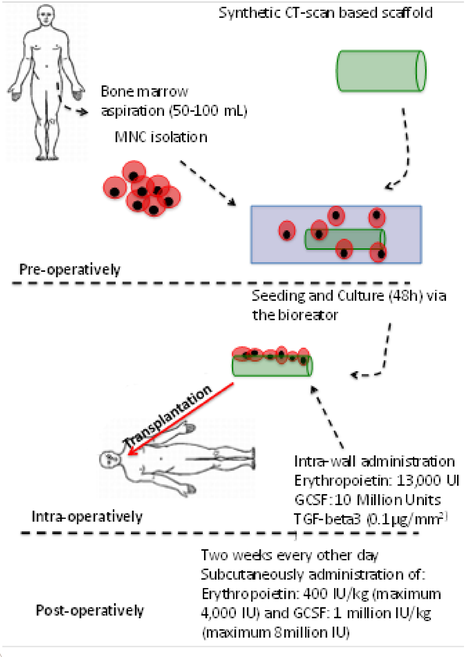
ABSTRACT

We have developed the first in the world synthetic nanofiber trachea that is combined with autologous stem cells and implanted into the patient to replace the damaged native trachea. Small polymer nanofibers were electrospun to form a tracheal prosthesis that was modeled from a CT scan of the patient. This nanofiber graft was then combined with bone marrow derived mononuclear cells from the patient and cultured two days *in vitro* before implantation into the patient. The autologous stem cells attached and proliferated on the highly porous and highly biocompatible nanofiber graft *in vitro* and the body was used as a bioreactor to differentiate the cells and create a fully functional trachea. Three surgeries have taken place to date, one in Sweden and two in Russia, with evidence of vascularization and functional epithelium one day post surgery. This synthetic nanofiber platform technology is currently being applied to replace other organs such as blood vessels, skin and small intestines and is changing the future of regenerative medicine and patient care.

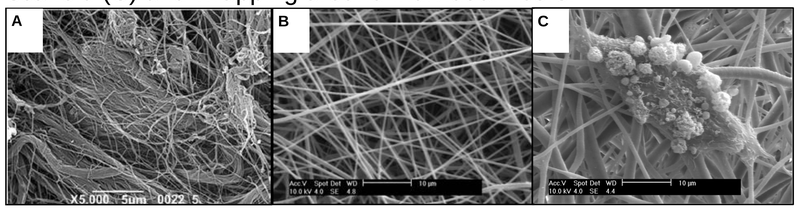
MATERIALS AND METHODS



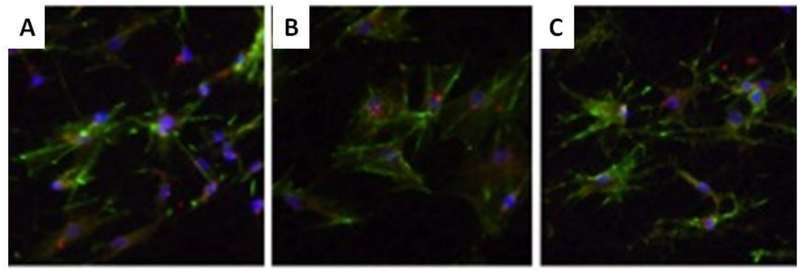
Autologous mononuclear cells (MNCs) were obtained 2 days before transplantation from a bone marrow aspirate through density gradient separation. Analyses of white blood cells, mononuclear cells, CD34+ cells, viability, colony forming unit-fibroblast, flow cytometry characterization, and sterility were done. Cells were resuspended in low-glucose DMEM and seeded onto the synthetic graft by incubation of the construct in a bioreactor at 37°C for 48 hrs before transplantation. The airway construct was transported to the operating theater and conditioned with growth and regenerative factors; recombinant human transforming growth factor-β3, granulocyte colony stimulating factor filgrastim (G-CSF), and epoetin beta (analogous synthetic of Erythropoietin). Sections of the graft were assessed by scanning electron, fluorescence, bright field, and confocal microscopy.

RESULTS - MICROSTRUCTURE

Scanning electron microscopy reveals the fibrous structure of native decellurized trachea (A) and the similarity with our nanofiber scaffold made from a blend of polyethylene terephthalate and polyurethane (B). A mesenchymal stem cell is shown growing on the nanofiber scaffold (C) and wrapping around individual fibers.

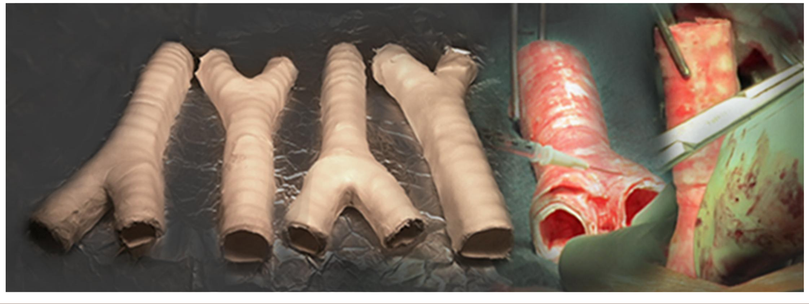


Fluorescence microscopy of mesenchymal stem cells cultured on the nanofiber scaffold with cells labeled for DNA (blue), actin (green) and CD90 (red) after 50 hrs of culture. Fibers were coated with collagen I (A), fibronectin (B) and poly-D-lysine (C).



RESULTS - MACROSTRUCTURE

Collage image of synthetic nanofiber tracheas after production (left) and after 2 days incubation with autologous stem cells immediately before implantation in the operating theater (right).



RESULTS – POST SURGERY

Photograph of tracheal graft sutured into position (left) and a representative bronchoscopy 3 days after the surgery (right). Notice the vascularization and tissue in-growth of the implanted synthetic trachea and lack of inflammatory response from the surrounding tissue demonstrating biocompatibility and acceptance of the nanofiber scaffold.

CONCLUSIONS – FUTURE WORK

Using synthetic nanofiber scaffolds to create artificial organs serves as a novel solution to the shortage of organ donations and problems associated with graft versus host disease. Seeding these scaffolds with appropriate biological sources, such as patient derived stem cells, results in fully functional organs that bypass organ availability and host compatibility issues. Nanofiber Solutions has created three artificial tracheas made from synthetic nanofibers and implanted into patients suffering from tracheal defects, but these events only begin to reveal the potential of nanofibers to transform the field of regenerative medicine and dramatically improve patient care. Future work involves tissue engineering of blood vessels, small intestines and skin.

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