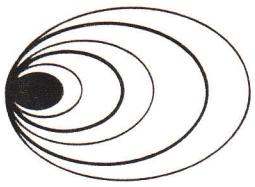

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SMALL-DIAMETER VASCULAR PROSTHESES WHICH RELEASE BIOACTIVE AGENTS.

The need for small-diameter vascular prostheses has been well documented by clinical experience which has shown poor graft patency rates with prostheses less than 6 mm internal diameter. Recently, substances which show considerable ability to stimulate endothelial cell proliferation in both capillaries and large vessels have been isolated and purified from a variety of tissues. It may be hypothesized that incorporating these substances into biocompatible materials could enhance endothelial cell development when these materials are used for fabrication of vascular prostheses. We have developed a spraying-phase inversion process which allows solutions of synthetic polymers or suspensions of synthetic and natural polymers to be blended and deposited over a rotating mandrel. With this method we have fabricated 1.5 mm ID, porous, compliant polyurethane tubes which incorporate and release basic fibroblast growth factor (bFGF). In vitro releasing studies were performed using 10% albumin by weight as carrier and which demonstrated 1-2 ng/cm graft/day rate of release of bFGF. The mitogenic effect of released bFGF was tested by incubating 1 cm long pieces of tubing with human endothelial cells seeded at low density (40 cells /mm^2) in vitro and using a culture medium without any growth factors added. The [^{3}H] thymidine uptake by the cells was measured. After 3 days the cells incubated with tubing that did not contain bFGF did not proliferate to any extent. Cells incubated with tubing that did contain bFGF continued to proliferate actively. The results of these experiments have shown that a bioactive bFGF can be released from vascular prostheses. Release of factors such as bFGF may enhance the early development of confluent endothelial surfaces in vivo that may increase thromboresistance of vascular prostheses.

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ANISODAMINE INHIBIT LUNG PLATELET SEQUESTRATION INITIATED BY EXTRACORPOREAL CIRCULATION (ECC)

Platelets are activated by the foriegn materials in ECC circuit and further trapped in lung leading to lung inflammatory response after ECC. This randomized study was aimed to show the in vivo effects of Anisodamine (654-2) on lung sequestration of platelets during ECC. 20 mongrel dogs were bypassed for 120 min with aorta cross-clamped for 90 min. No blood were transfused. The treated dog had 654-2 infusion in a total dose of 15 mg/kg while the control was treated with normal saline only.

During ECC, the difference of platelet numbers between left atrium (A) and right atrium(V) in both groups around the time period of cross-clamp release (X-release) are shown:

Group		Before X-release	5 min X-release	15 min X-release
654-2	(A)	62.3±7.9	52.9±5.8	59.8±6.7
(n=10)	(V)	52.4±5.7	48.4±4.5	54.9±7.2
Control	(A)	44.4±12.5	35.9±6.9	30.0±5.2
(n=10)	(V)	47.4±6.3	47.9±8.1**	46.4±6.3**

** = P<0.01 A vs V, Mean±SEM

In addition, the lung histological findings showed much less platelets trapped in pulmonary microvasculatures in 654-2 group dogs (P<0.01).

It has been proved that 654-2 may protect pulmonary non-respiratory function of disaggregating platelets. This study imply that the lung platelet sequestration during ECC may possibly be protected by the prophylactic use of 654-2.

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THE MICROPOROUS TRACHEAL PROSTHESIS

Since complete incorporation of a tracheal prosthesis with an epithelial lining seems to be required to prevent infection and granuloma formation, we developed a polyurethane reinforced microporous tubular graft of 20 mm ID and 8 cm length for implantation in the cervical part of the trachea of a goat.

Trachea Prosthesis	N	Infection	Granuloma
microporous controls	7	5	7
+cuff technique	9	4	3
+peritoneum lining	3	3	3
+artificial skin lining	3	3	3
+preimplanted + mesh graft	6	3	6

The results indicate that a cuff technique is needed to reduce anastomotic granuloma formation. The artificial skin as well as vital peritoneum were able to prevent infection to occur in the first 2 weeks, but not thereafter because of loosening of the layers. Preimplanted mesh grafted trachea epithelium did not completely cover the graft within 2 weeks, but showed a certain resistance to infection already after interposition.

In conclusion: Microporous material permits complete epithelialization in a non-contaminated area (subcutaneous preimplantation). Prevention of anastomotic granuloma formation requires a non exposure of the anastomosis to the airway (cuff technique). Complete epithelialization is needed t prevent infection of the prosthesis.

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A NEWLY DEVISED HEMOSTATIC MATERIAL "GTXIII"

GTXIII, comprising biodegradable gelatin (G) as a drug carrier of thrombin (T) and blood coagulation factor XIII (XIII).

Thrombin converts fibrinogen into soluble fibrin (SF) and "SF" is converted into insoluble fibrin (ISF) by transglutamidase activity of "XIII". In this mechanism "T" and "XIII" perform essential function to complete hemostasis.

In order to investigate the hemostatic activity of "GTXIII" we studied ①Weights of "SF", "ISF" and blood coagula (BC) formed by reactions of "GTXIII" with fibrinogen solution and whole blood, respectively. These experiments were performed periodically at reaction times (RT) of 0.5, 1, 2 and 5 mins. ②"GTXIII" was injected as a sol state into a punctured site of liver biopsy for warfarinized rats. Times taken for complete hemostasis (Hemostatic Time, (HT)) were measured. In these experiments ① and ② three different types of materials were tested as well as "GTXIII". Namely, those are "G", "G" & "T" (GT) and "G" & "XIII" (GXIII). Results were compared with "GTXIII" as follows.

Samples	SF(mg)	ISF(mg)	BC(mg)	HT(mins)
GTXIII	31.0	29.5	59.9	1.7
G	22.1 #	9.9 #	41.2 #	10.0 #
GT	28.9 #	13.0 #	50.7 #	10.0 #
GXIII	29.1 #	24.2 #	43.0 #	10.0 #

# p<0.05, * p<0.1, RT=2 mins

These data confirm that "XIII" is essential for the formation of "ISF" and "BC" and that increase of topical concentrations of both "T" and "XIII" at the bleeding site is very much effective for hemostasis.

In summary, "GTXIII" is expected to have various clinical uses as a hemostatic, as a thrombotic agent in sclerotherapy and trans-catheter embolization and as an accelerant in wound healing.

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