

# Project Information ?

1R01HL084080-01A1

DESCRIPTION DETAILS RESULTS HISTORY SUBPROJECTS

**Project Number:** 1R01HL084080-01A1  
**Title:** THROMBIN DYSREGULATION LEADS TO EARLY SAPHENOUS VEIN GRAFT FAILURE  
**Contact PI / Project Leader:** [POSTON, ROBERT S.](#)  
**Awardee Organization:** UNIVERSITY OF MARYLAND BALTIMORE

**Abstract Text:**

DESCRIPTION (provided by applicant): Saphenous vein graft (SVG) closure after coronary artery bypass grafting (CABG) is an underreported and poorly understood problem. Imperfect surgical technique is frequently blamed but this can be detected using flow measurement technology, allowing us to focus on other causal factors. We have developed clinical tools to show that endothelial cell (EC) disruption in the saphenous vein graft (SVG) and aspirin resistance (ASA-R) after CABG are significant predictors of graft failure. Analysis of coronary sinus (CS) blood samples obtained from these patients revealed that the level of F1.2, a marker of thrombin formation, relates to ASA- R and abnormalities of blood flow and EC integrity in the SVG (i.e. Virchow's triad). On the basis of this and other observations, we hypothesize that a dysregulated burst of thrombin within the SVG is a common pathway in the development of graft failure. This hypothesis will be tested first with an animal model in order to establish that controlled manipulations in SVG thrombogenicity and the other components of Virchow's triad have a consistent and measurable impact of thrombin within the SVG. We have developed a comprehensive strategy for analyzing the role of thrombin in our porcine CABG model by monitoring its stimulus (tissue factor), formation (F1.2 peptide release), deposition (activity assessed directly on the SVG lumen), effects (imaging of mural thrombus and analysis of platelet derived microparticles) and inhibition (TAT complex). Novel approaches to prevent thrombin production within the high risk SVG will be tested. Because it is difficult to model ASA-R and other common clinical risk factors for SVG thrombosis in animals, a sufficiently powered clinical trial will be required to establish the link between a burst in thrombin production within the SVG and early graft failure. Lay Description: Familiarity, concerns about the safety of alternatives, and acceptable intermediate-term results have led to established practice patterns such as use of aspirin as the sole antiplatelet agent and routine use of the SVG as a conduit for most bypass cases. Definitive alterations in management strategies after CABG await a clear understanding of why grafts fail and the elucidation of treatable risk factors, e.g. regional thrombin dysregulation. Because anticoagulation is not harmless in these patients, reliable identification of the risk of SVG failure would provide a rationale basis to selectively intervene and optimize graft patency without increasing bleeding in the population as a whole.

**Project Terms:**

Accounting; Animal Model; Animals; Anticoagulation; Antiplatelet Drugs; Aspirin; base; Biological Assay; Blood; Blood flow; Blood Platelets; Blood specimen; Bypass; catalyst; cell injury; Clinical; Clinical Research; Clinical Trials; Closure; Coagulation Process; Complex; Coronary Artery Bypass; Coronary sinus structure; day; Defect; Deposition; Development; Disruption; Endothelial Cells; Exclusion; Familiarity; Family suidae; Feedback; Fibrinolytic Agents; Future; graft failure; Hemorrhage; Hour; Human; Image; Intravascular Thrombus Formation; Lead; Link; Measurable; Measurement; Mediating; Modeling; Monitor; novel; novel strategies; Operative Surgical Procedures; Pathway interactions; Patients; Pattern; Peptides; Platelet Function Tests; Population; Postoperative Period; prevent; Production; programs; Prothrombin; Regulation; Research Personnel; Resistance; Risk; Risk Factors; Role; Safety; Saphenous Vein; Stimulus; Stress; Sus scrofa; Techniques; Technology; Testing; Thrombin; Thromboplastin; Thrombosis; Thrombus; Time; tool; Translating; Translations; Triad Acrylic Resin; Work

<b>Contact PI Information:</b>	<b>Program Official Information:</b>	<b>Other PI Information:</b>
<b>Name:</b> POSTON, ROBERT S. <b>Email:</b> <a href="#">Click to view contact PI email address</a> <b>Title:</b> CHIEF, CARDIOTHORACIC SURGERY	<b>Name:</b> HASAN, AHMED A.K. <b>Email:</b> <a href="#">Click to view PO email address</a>	Not Applicable

<b>Organization:</b>	<b>Department / Educational Institution Type:</b>	<b>Congressional District:</b>
<b>Name:</b> UNIVERSITY OF MARYLAND BALTIMORE <b>City:</b> BALTIMORE <b>Country:</b> UNITED STATES (US)	SURGERY SCHOOLS OF MEDICINE	State Code: MD District: 07

**Other Information:**

<b>FOA:</b>	<b>DUNS Number:</b> 188435911	<b>CFDA Code:</b> 837
<b>Study Section:</b> Clinical and Integrative Cardiovascular Sciences Study Section (CICS)	<b>Project Start Date:</b> 1-FEB-2007	<b>Project End Date:</b> 31-JAN-2012
<b>Fiscal Year:</b> 2007 <b>Award Notice Date:</b> 31-JAN-2007	<b>Budget Start Date:</b> 1-FEB-2007	<b>Budget End Date:</b> 31-JAN-2008

**Administering Institutes or Centers:**  
 NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

**Project Funding Information for 2007:**

**Total Funding:** \$545,579

Year	Funding IC	FY Total Cost by IC
2007	NATIONAL HEART, LUNG, AND BLOOD INSTITUTE	\$545,579

INSTITUTE

**History:**

Project Number	Sub #	Project Title	Contact Principal Investigator	Organization	FY	Admin IC	Funding IC	FY Total Cost by IC
7R01HL084080-05		THROMBIN DYSREGULATION LEADS TO EARLY SAPHENOUS VEIN GRAFT FAILURE	POSTON, ROBERT S.	UNIVERSITY OF ARIZONA	2011	NHLBI	NHLBI	\$483,735
5R01HL084080-04		THROMBIN DYSREGULATION LEADS TO EARLY SAPHENOUS VEIN GRAFT FAILURE	POSTON, ROBERT S.	BOSTON MEDICAL CENTER	2010	NHLBI	NHLBI	\$401,893
7R01HL084080-03		THROMBIN DYSREGULATION LEADS TO EARLY SAPHENOUS VEIN GRAFT FAILURE	POSTON, ROBERT S.	BOSTON MEDICAL CENTER	2009	NHLBI	NHLBI	\$363,215
5R01HL084080-02		THROMBIN DYSREGULATION LEADS TO EARLY SAPHENOUS VEIN GRAFT FAILURE	POSTON, ROBERT S.	UNIVERSITY OF MARYLAND BALTIMORE	2008	NHLBI	NHLBI	\$473,219
1R01HL084080-01A1		THROMBIN DYSREGULATION LEADS TO EARLY SAPHENOUS VEIN GRAFT FAILURE	POSTON, ROBERT S.	UNIVERSITY OF MARYLAND BALTIMORE	2007	NHLBI	NHLBI	\$545,579

**Subprojects:**

Project Number	Sub #	Project Title	Contact Principal Investigator	Organization	FY	Admin IC	FY Total Cost by IC
No Subprojects information available for 1R01HL084080-01A1							

Page Last Updated on May 22, 2016  
 This site is best viewed with Internet Explorer (8.0 or higher) or Mozilla Firefox (11.0 or higher).

NIH...Turning Discovery Into Health®

RePORTER3N