

PATENT ASSIGNMENT COVER SHEET

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SUBMISSION TYPE:	NEW ASSIGNMENT	
NATURE OF CONVEYANCE:	ASSIGNMENT	
CONVEYING PARTY DATA		
	Name	Execution Date
	THE UNIVERSITY OF READING	11/02/2016
RECEIVING PARTY DATA		
Name:	WESTERN NEW ENGLAND UNIVERSITY	
Street Address:	1215 WILBRAHAM RD	
City:	SPRINGFIELD	
State/Country:	MASSACHUSETTS	
Postal Code:	01119	
PROPERTY NUMBERS Total: 1		
	Property Type	Number
	Application Number:	16480844
CORRESPONDENCE DATA		
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<i>Correspondence will be sent to the e-mail address first; if that is unsuccessful, it will be sent using a fax number, if provided; if that is unsuccessful, it will be sent via US Mail.</i>		
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NAME OF SUBMITTER:	ROBERTA L. PELLETIER	
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DATE SIGNED:	07/30/2019	
Total Attachments: 16 source=8C65934#page1.tif source=8C65934#page2.tif source=8C65934#page3.tif source=8C65934#page4.tif source=8C65934#page5.tif		

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ASSIGNMENT

THIS AGREEMENT IS DATED OCTOBER 31, 2018

PARTIES

- (1) WESTERN NEW ENGLAND UNIVERSITY, a Massachusetts 501(c)(3) Nonprofit Corporation having an address at 1215 Wilbraham Road, Springfield, Massachusetts ("WNE"); and
- (2) THE UNIVERSITY OF READING, a corporation with charitable status, established by Royal Charter with company number RC000885, whose administrative offices are at Whiteknights House, Whiteknights, PO Box 217, Reading, Berkshire, RG6 6AH, United Kingdom ("Reading").

BACKGROUND

- (1) Dr Dan Kennedy ("Inventor 1") and Professor Jon Gibbins and Lisa Marie Holbrook (collectively "Inventors 2") conceived, created and made the invention (as defined in Schedule 1) whilst Inventor 1 was an employee of WNE and whilst Jon Gibbins was an employee of Reading and whilst Lisa Marie Holbrook was a post-doctoral research associate at Reading;
- (2) WNE and Reading are joint owners of the invention because in the absence of any collaboration agreement the default legal position of joint ownership applies;
- (3) WNE would like to own all right, title and interest in the invention and file one or more patent applications directed at the invention (which may include filing an application in its own name naming at least inventor 1 and inventors 2 as inventors), and Reading agrees with this course of action;
- (4) Reading is willing to assign all its right, title and interest in its share of the invention to WNE subject to the provisions of this Agreement; and
- (5) WNE is willing to take assignment of Reading's share of the invention and to commercialise the invention or to find a commercial partner to develop a commercial product which falls under the claims of such patent applications or granted patents based on such patent applications.

NOW, THEREFORE, based upon the foregoing and other good and valuable consideration, the receipt and sufficiency of which hereby is acknowledged, and intending to be legally bound hereby, the Parties agree as follows.

AGREED TERMS

1 ASSIGNMENT

- 1.1 Reading hereby irrevocably assigns and transfers to WNE absolutely, all of its right, title and interest in the invention and all intellectual property rights in such invention with full effect from the date of this Agreement. For the avoidance of doubt, the assignment of Reading's right, title and interest in the invention shall not be taken to mean that future inventions outside the scope of the invention shall automatically belong to WNE. Future inventions outside the scope of the invention made by Inventors 2 as employees of Reading shall belong to Reading and Reading will be free to offer these inventions to any third party.
- 1.2 The assignment effected by this Clause 1 shall include the assignment and transfer of:
 - 1.2.1 all rights to file patent applications directed at the invention as set out in Schedule 1, as well as all patents and other similar registered rights that are directed at the invention or any part of the invention in any country of the world (including continuations, continuations-in-part, extensions, re-examinations, reissues, divisional applications, and supplementary protection certificates);
 - 1.2.2 the right to claim priority from any patent application;
 - 1.2.3 the right to apply for a patent or other similar registered right in any territory or group of territories in respect of the invention; and
 - 1.2.4 all rights of action, powers and benefits arising from ownership of the invention and any patents directed at the invention or any part of the invention, including without limitation the right to sue for damages and other legal and equitable remedies in respect of all causes of action arising prior to, on or after the date of this Agreement.
- 1.3 Reading shall promptly execute such documents and give such reasonable assistance as WNE may require, at WNE's expense:
 - 1.3.1 to secure the vesting in WNE of all rights in the invention and any patent directed at the invention or any part of the invention;
 - 1.3.2 to assist in obtaining and defending the grant of all patents or similar registered rights in the invention or any part of the invention;
 - 1.3.3 to uphold WNE's rights in the invention and any patent directed at the invention or any part of the invention; and

1.3.4 to defeat any challenge to the validity of, and resolve any questions concerning, the invention and any patent directed at the invention or any part of the invention.

1.4 For purposes of clarity, notwithstanding anything in this Agreement or any other agreement between the Parties to the contrary, (i) Reading is not assigning any right, title or interest in or to any assay (and any other tests, methods or apparatus) which is set out in the Proposal jointly prepared by Inventor 1 and Jon Gibbons (as part of Inventors 2, a copy of which is attached hereto as Schedule 2, and the assignment under this Agreement with respect to the invention is solely an assignment of Reading's share of the invention and (ii) nothing in this Agreement or any other agreement between the Parties limits, restricts or otherwise prevents Reading from using or applying the assay (or any other tests, methods or apparatus) described in the Proposal for any purpose, whether for commercial purposes, for research or any other purposes.

2 WNE'S OBLIGATIONS

2.1 WNE undertakes to use commercially reasonable efforts to commercialise the invention or to find a commercial partner to develop a commercial product according to the invention.

2.2 WNE will annually provide Reading with such information that Reading may reasonably request to demonstrate that WNE (or WNE's commercial partner) is commercialising or is taking reasonable steps towards commercialising the invention. If WNE cannot demonstrate that it is commercialising the invention or any part of the invention or is taking reasonable steps towards commercialising the invention or any part of the invention, WNE will, if reasonably requested to do so by Reading and if WNE is not otherwise prevented from doing so by any non-negotiable terms under one or more agreements with third parties related to the development or commercialization of the invention, assign back to Reading the right, title and interest in the invention (including patents directed to the invention) that Reading assigned to WNE in Section 1.1, provided, however, as a condition to such assignment, Reading would reimburse WNE for 50% of the fees, costs and expenses (including attorney's fees) incurred by WNE in connection with the preparation, filing, prosecution and maintenance of such patents directed at the invention, provided, further, however, notwithstanding anything in this Agreement to the contrary, in the event WNE sells, assigns or transfers the invention to a third party, any obligations of WNE to assign any rights in the invention back to Reading or continue to report progress on any commercialization steps taken are hereby terminated. Reading acknowledges and agrees that the invention, being directed to a pharmaceutical application, will require several years to develop and commercialize,

during which time further development may be undertaken, clinical testing may be undertaken, regulatory approvals may be required to be obtained, agreements with third party partners may need to be negotiated and executed, and the like, and Reading agrees that the undertaking of these or similar steps, individually and in the aggregate, demonstrates that WNE (or WNE's commercial partner) is commercialising or is taking reasonable steps towards commercialising the invention.

- 2.3 Should WNE succeed in commercialising the invention or any part of the invention by way of selling a product or service, or deriving an income stream from a licence to any patent directed at the invention or any part of the invention, or by any other method, including the sale, assignment or transfer of the invention to a commercial partner through arm's length negotiation, WNE shall enter into an agreement with Reading for the payment of royalties, a lump sum payment and/or a contribution in kind received by WNE to Reading arising from such commercialisation of the invention. It is expected that the profits will be split equally between the Parties taking into account any financial contributions which WNE (or Reading) may have made to further develop and commercialise the invention. Such agreement shall be agreed between Reading and WNE acting in good faith, through commercial, arm's length negotiations. Should the Parties fail to agree the terms of such an agreement the Parties will follow the process set out in Clause 12.
- 2.4 Should WNE wish to sell, assign or transfer the invention to a third party, other than a commercial partner, for example to an entity that specialises in finding commercial partners for university inventions, WNE is free to do so, however, WNE may novate this Agreement to such a third party only with Reading's prior written consent; such consent not to be unreasonably delayed or withheld.

3 RESEARCH LICENSE

- 3.1 Unless WNE is prevented from doing so by any non-negotiable terms under one or more agreements with third parties related to the development or commercialization of the invention, WNE hereby grants to Reading and to Inventors 2 a non-exclusive, royalty-free, world-wide license to use the invention for the sole purpose of academic teaching and research, including research projects that are sponsored by any third party provided that any such third party gains and claims no rights to the invention. The rights in this clause are subject to the rules on publication in Clause 4.

4 CONFIDENTIALITY AND PUBLICATIONS

- 4.1 For the purpose of this Agreement "Confidential Information" shall mean in relation to each Party any materials, trade secrets or other information of a confidential nature

disclosed by one Party to the other as a result of this Agreement and which is identified as confidential before (either verbally or in writing) or at the time of disclosure and "FOI Legislation" shall mean the English Freedom of Information Act 2000 (as amended), the Environmental Information Regulations 2004 (as amended), and the INSPIRE Regulations 2009. For the avoidance of doubt, the Invention shall be considered to be WNE's Confidential Information.

- 4.2 Subject to Clauses 4.5, the Parties shall use all reasonable endeavours not to disclose to any third party any Confidential Information nor use for any purpose except as expressly permitted by this Agreement, any of the other Party's Confidential Information.
- 4.3 No Party shall incur any obligation under Clause 4.2 with respect to information which:
 - 4.3.1 is known to the receiving Party before the start of the date of this Agreement, and not impressed already with any obligation of confidentiality to the disclosing Party, provided, however, with respect to the Invention, this exclusion does not apply to inventors 2 or Reading because the Invention was known to each before the start of the date of this Agreement;
 - 4.3.2 is or becomes publicly known without the fault of the receiving Party;
 - 4.3.3 is obtained by the receiving Party from a third party in circumstances where the receiving Party has no reason to believe that there has been a breach of an obligation of confidentiality owed to the disclosing Party;
 - 4.3.4 is independently developed by the receiving Party;
 - 4.3.5 is approved for release in writing by an authorised representative of the disclosing Party; or
 - 4.3.6 the receiving Party is specifically required to disclose in order to fulfil an order of any Court of competent jurisdiction provided that, prior to such disclosure (other than in connection with a request under the FOI Legislation, the process for which is set out in Section 4.4) the receiving Party notifies the other Party in writing so as to allow the other Party to seek a protective order or other remedy to prevent or limit such disclosure, and in the case of a disclosure made under the FOI Legislation, none of the exemptions or exceptions contained in the FOI Legislation apply to the Confidential Information.
- 4.4 If a Party receives a request under the FOI Legislation to disclose any information of the other Party, it shall notify and consult with the Party to whom the information belongs. The other Party shall respond within five (5) working days after receiving notice of the request for information, setting out whether or not it considers that an exemption or

exception under the FOI Legislation applies, the reasons for this assertion and providing all necessary assistance as reasonably requested to enable the Party to respond to the request for information within the time for compliance as set out in the FOI Legislation. The Party that receives the request for information shall, however, be responsible for determining in its absolute discretion whether the information requested is exempt from disclosure in accordance with the FOI Legislation.

- 4.5 Reading shall submit to WNE, in writing, details of any planned publication (including any thesis which a student intends to submit) which discloses the invention or any part of the invention that any employee, student, agent or appointee of Reading intends to publish, not less than thirty (30) days in advance of the submission for publication. WNE may, by giving written notice to Reading (a "Confidentiality Notice") require Reading to delay the proposed publication for a maximum of six (6) months from the date of receipt of the Confidentiality Notice, if in the reasonable opinion of WNE, such a delay is necessary in order to seek patent or similar protection for the invention or any part of the invention that are to be published. WNE must issue a Confidentiality Notice to Reading within thirty (30) days after WNE receives details of the proposed publication. If Reading does not receive a Confidentiality Notice within that period, its employee, student, agent or appointee may proceed with the proposed publication.
- 4.6 The provisions of Clauses 4.2 and 4.5 shall survive for a period of five (5) years from the date of termination of this Agreement.

5 WARRANTIES, INDEMNITY AND LIMIT OF LIABILITIES

- 5.1 Each Party warrants to the other Party that it has legal power, authority and right to enter into this Agreement and to perform its respective obligations in this Agreement.
- 5.2 Reading hereby warrants to WNE at the date of this Agreement that:
 - 5.2.1 it is entitled to assign its rights to its share of the invention to WNE and all employees and students (including post-doctoral research associates) of Reading that took part in the conception, creation or making of the invention have assigned their respective rights to the invention to Reading such that Reading is able to fully assign its rights to its share of the invention to WNE;
 - 5.2.2 it has not previously assigned or licensed all or any rights to its share of the invention or entered into any agreement relating to its share in the invention, which might affect its ability to assign its share in the invention to WNE;
 - 5.2.3 it is not aware any allegations or proceedings, pending or threatened, which assert that the invention infringes or will infringe third party rights; and

- 5.2.4 It is not aware of any third party contractual relationship which may affect WNE's full and complete exercise of rights under this Agreement.
- 5.3 In the event of Reading becoming aware of any information which might effect the warranties set out above it will promptly inform WNE.
- 5.4 OTHER THAN THE EXPRESS WARRANTIES SET OUT IN SECTIONS 5.1 AND 5.2, READING DISCLAIMS ANY AND ALL WARRANTIES, EXPRESS OR IMPLIED, RELATED TO THE INVENTION. READING DISCLAIMS ANY AND ALL WARRANTIES, EXPRESS OR IMPLIED, RELATED TO THE INVENTION. WITHOUT LIMITING THE GENERALITY OF THE FOREGOING, Reading does not give any warranty:
- 5.4.1 that any patent application directed at the invention will proceed to grant;
- 5.4.2 that the invention is fit for a particular use;
- 5.4.3 that the invention does not infringe the rights of any third party;
- 5.4.4 that any information communicated by Reading to WNE under or in connection with the invention will produce products of satisfactory quality or will be fit for a particular purpose; or
- 5.4.5 as imposing any obligation on Reading to bring or prosecute actions or proceedings against third parties for infringement or to defend any action or proceedings for revocation of any patent directed at the invention.
- 5.5 Subject to Clause 5.11 and except under the limited warranty in Clause 5.2 and the indemnity in Clause 5.7, neither Party accepts any responsibility for any use which may be made by the other Party of the invention, nor for any reliance which may be placed by that other Party on the invention, nor for advice or information given in connection with the invention.
- 5.6 WNE (or its commercial partner) or, in the case that the Agreement is novated in accordance with Clause 2.4, the third party (or their commercial partner) will be responsible for the design and manufacture of products according to the invention and that Reading has no responsibility or liability in that respect.
- 5.7 WNE will indemnify, defend and hold harmless Reading and every employee, officer and student of Reading (the "Indemnified Parties"), and keep them fully and effectively indemnified, against each and every claim made by a third party against any of the Indemnified Parties as a result of WNE's (or WNE's commercial partner's) manufacture, use, sale of or other dealing in any product according to the invention or under any patent directed at the invention, provided that the Indemnified Party must:
- 5.7.1 promptly notify WNE of details of the claim;

- 5.7.2 not make any admission in relation to the claim;
- 5.7.3 allow WNE to have sole control over the conduct of the defence or settlement of the claim, provided, however, any settlement shall not include any obligations on the part of the Indemnified Party and shall not include any admission of liability of any kind by the Indemnified Party; and
- 5.7.4 give WNE all reasonable assistance (at WNE's expense) in dealing with the claim.

The indemnity in this Clause will not apply to the extent that the claim arises as a result of the Indemnified Party's gross negligence, the deliberate breach of any agreement between Reading and WNE, or any breach of confidence.

5.8 [Intentionally Omitted]

- 5.9 Subject to Clause 5.11 and except under the indemnity in Clause 5.7 or a breach under Clause 4, the liability of a Party to the other Party for any breach of this Agreement, any negligence or arising in any other way out of the subject matter of this Agreement, will not extend to any indirect, special, consequential or pure economic damages or losses, or any loss of profits, loss of revenue, loss of data, loss of contracts or opportunity, whether direct or indirect, even if the Party bringing the claim has advised the other of the possibility of those losses, or if they were within the other Party's contemplation.
- 5.10 Subject to Clause 5.11 and except under the limited warranty in Clauses 5.2 and the indemnity in Clause 5.7 or a breach under Clause 4, the aggregate liability of each Party to the other for all and any breaches of this Agreement, any negligence or arising in any other way out of the subject matter of this Agreement, will not exceed in total \$100,000 (one hundred thousand dollars US).
- 5.11 Nothing in this Agreement limits or excludes either Party's liability for:
 - 5.11.1 death or personal injury resulting from negligence; or
 - 5.11.2 any fraud or for any sort of liability that, by law, cannot be limited or excluded.
- 5.12 Each of the Parties acknowledges that, in entering into this Agreement, it has not relied on any warranty, representation or undertaking except those expressly set out in this Agreement and each Party waives any claim for breach of any representation (unless made fraudulently) which is not specifically contained in this Agreement as a warranty.

8 EXECUTION

- 6.1 This Agreement may be executed in any number of counterparts, each of which when executed (and delivered) will constitute an original of this Agreement, but all counterparts will together constitute the same Agreement. No counterpart will be effective until each Party has executed at least one counterpart.

7 SEVERABILITY

- 7.1 If any provision or part provision of this Agreement is or becomes invalid, illegal or unenforceable, it shall be deemed modified to the minimum extent necessary to make it valid, legal and enforceable. If such modification is not possible, the relevant provision or part-provision shall be deemed deleted. Any modification to or deletion of a provision or part-provision under this Clause shall not affect the validity and enforceability of the rest of this Agreement.
- 7.2 If any provision or part-provision of this Agreement is invalid, illegal or unenforceable, the Parties shall negotiate in good faith to amend such provision so that, as amended, it is legal, valid and enforceable and to the greatest extent possible, achieves the intended commercial result of the original provision.

8 NOTICES

- 8.1 Any notice given under this Agreement shall be in writing, sent for the attention of the person, and to the address set out below (or such other address or person as the relevant Party may notify to the other Party) and shall be delivered either:
- 8.1.1 personally;
 - 8.1.2 by courier;
 - 8.1.3 by pre-paid, first-class post; or
 - 8.1.4 by recorded delivery.
- 8.2 A notice is deemed to have been received: if delivered personally, at the time of delivery; in the case of pre-paid first class post, recorded delivery or courier, forty eight (48) hours from the date of posting. If deemed receipt under this Clause 8.2 is not within two (2) working days, the notice will be deemed to be received at the commencement of normal working hours on the first working day following delivery. To prove service of notice, it is sufficient to prove that the envelope containing the notice was properly addressed and posted or handed to the courier.

For WNE:

Evan T. Robinson, R.Ph., Ph.D.
Dean and Associate Provost for Academic Affairs
Western New England University College of Pharmacy
1215 Wilbraham Road
Springfield, MA 01119

With a copy to:

Cheryl I. Smith
General Counsel
Western New England University
1215 Wilbraham Road
Springfield, MA 01119

For Reading:

Head of Commercialisation
Research & Enterprise
The University of Reading
Room 201 Whiteknights House
Whiteknights Campus
Reading
RG6 6AH
United Kingdom

9 HEADINGS

- 9.1 Clause and schedule headings are for ease of reference only and do not affect the interpretation of this Agreement.

10 ENTIRE AGREEMENT

- 10.1 This Agreement constitutes the entire agreement between the Parties and supersedes and extinguishes all previous agreements, promises, assurances, warranties, representations and understandings between them, whether written or oral, relating to its subject matter.

11 VARIATION

- 11.1 Any variation of or amendment to this Agreement shall only be effective if it is in writing and signed by both Parties.

12 DISPUTE RESOLUTION

- 12.1 The Parties shall use good faith efforts to resolve disputes, within twenty (20) business days of notice of such dispute. Such efforts shall include escalation of such dispute to the corporate officer level of each Party. If the Parties cannot resolve any such dispute within said twenty (20) business day period, the matter shall be

submitted to arbitration for resolution. Arbitration will be conducted in Boston, Massachusetts shall be initiated by filing a demand at the Boston, Massachusetts regional office of the American Arbitration Association ("AAA"). Disputes will be heard and determined by a single arbitrator, who will have significant experience in resolving intellectual property related matters. Within fifteen (15) business days following the selection of the arbitrator, the Parties shall present their claims to the arbitrator for determination. Within ten (10) business days of the presentation of the claims of the Parties to the arbitrator, the arbitrator shall issue a written opinion. To the extent the matters in dispute are provided for in whole or in part in this Agreement, the arbitrator shall be bound to follow such provisions to the extent applicable. In the absence of fraud, gross misconduct or an error in law appearing on the face of the determination, order or award issued by the arbitrator, the written decision of the arbitrator shall be final and binding upon the Parties.

13 GOVERNING LAW AND JURISDICTION

13.1 Subject to Section 12, this Agreement shall be governed by the laws of the Commonwealth of Massachusetts, without application of conflicts of law principles, and the state and federal courts of the Commonwealth of Massachusetts shall have exclusive jurisdiction to deal with any dispute which may arise out of or in connection with this Agreement.

14 THIRD PARTY RIGHTS

14.1 This Agreement is for the sole benefit of the Parties hereto and their respective successors and permitted assigns and nothing herein, express or implied, is intended to or shall confer upon any other person or entity any legal or equitable right, benefit, or remedy of any nature whatsoever, under or by reason of this Agreement, and a person who is not party to this Agreement shall have no right under the Contracts (Rights of Third Parties) Act 1999 to enforce any term of this Agreement.

15 MISCELLANEOUS

15.1 WNE (and WNE's commercial partner) shall not use the name or any trademark or logo of Reading or the name of any of its staff or students in any press release or product advertising, or for any other commercial purpose or in any activities which implies endorsement of WNE's (or WNE's commercial partner's) business and/or activities, without the prior written consent of Reading.

15.2 For purposes of clarity, nothing in this Agreement prevents WNE from assigning or transferring the invention to a third party. WNE shall have the right to assign this

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Agreement to any commercial partner who is an assignee or transferee of the
Invention.

EXECUTED as an agreement:

SIGNED for and on behalf of THE UNIVERSITY OF READING

Name: THE UNIVERSITY OF READING
MIRANDA JOYCE
Position: CONTRACTS MANAGER

Signature: *M. Joyce* 2/Nov/2016

SIGNED for and on behalf of WESTERN NEW ENGLAND UNIVERSITY

Name: *Ewan T. Robinson*

Position: *Dean + Associate Provost*

Signature: *ET Robinson*

SCHEDULE 1

Invention

All inventions, ideas, concepts, compositions of matter, techniques, processes, improvements, developments, discoveries, know-how, technical information and data related to the use of the Compounds (as defined below) for use in any therapeutic area that is associated with the inhibition or modulation of thiol isomerases or any member of the thiol isomerases family of enzymes (such as ERp57, Protein disulfide isomerase (PDI), and ERp5), including but not limited to the areas of arterial and venous thrombosis, cancer, HIV or any other infectious diseases, immune disorders and neurologic diseases.

"Compounds" means the following known pharmaceutical compounds: Zafirlukast, Montelukast, oxcarbazepine, Mesalazine, Balsalazide, Benserazide, Butaciamol, Alosetron and l-dopa.

RE007996

SCHEDULE 2

Proposal



20161026 proposal
RE008532.docx

GSK Discovery Challenge: Development of an ERp57 inhibitor to prevent arterial and venous thrombosis

The therapeutic hypothesis

We have discovered that the thiol isomerase enzyme Erp57 plays a fundamentally important role in the regulation of platelet function. This is important because while platelets perform an important protective role to prevent bleeding following injury, their inappropriate activation in diseased blood vessels is the principle trigger for thrombosis. Thrombosis causes heart attacks and strokes, that represent the most prevalent causes of death and morbidity in the developed world.

ERp57 is released by platelets following their activation and upon tissue damage whereupon it binding to the platelet surface, and particularly to integrin receptors. Through a mechanism that is believed to involve the oxidation, reduction and isomerisation of disulphide bonds in receptors, and particularly integrins such as $\alpha IIb\beta 3$, ERp57 plays important roles in regulating initial platelet activation, intracellular calcium mobilization, granule secretion, fibrinogen binding, aggregation and thrombus formation. The inhibition of extracellular thiol isomerases such as ERp57 has also been shown to result in diminished tissue factor activity following exposure at site of injury. ERp57 inhibition therefore holds the potential to not only inhibit platelet function, but to also reduce thrombosis through reduction of coagulation. This opens up ERp57 as a potential dual anti-thrombotic target with the ability to reduce arterial (largely platelet driven) and venous (largely coagulation driven) thrombosis. This would offer a significant improvement over currently available therapies that only target prevention of either arterial (aspirin, clopidogrel) or venous (warfarin, dabigatran, rivaroxaban) thrombosis. Pharmaceuticals directed against thiol isomerases have been reported to represent a novel anti-thrombotic strategy.

To test this we have developed antibodies that selectively inhibit ERp57 enzymatic activity. On exposure to these antibodies platelet responses to endogenous agonists are reduced, and infusion into the circulation of mice protects them from laser induced arterial thrombosis. The use of antibody therapies for prophylaxis is not practical and therefore selective ERp57 inhibitors are required to explore the targeting of this protein as a new therapeutic approach.

Description of the target

ERp57 is a member of the family of oxidoreductases that normally function in the endoplasmic reticulum to facilitate disulphide bond isomerisation to chaperone correct protein folding. While each member will possess substrate selectivity, with respect to haemostasis and thrombosis there exists some functional redundancy between family members and therefore inhibition or deletion of ERp57 (in transgenic mice) is well tolerated and is not associated with excessive bleeding. In platelets ERp57 is released to the cell surface where its chaperone protein function (and probably structure) modulates platelet activation. Extracellular thiol isomerases have also been implicated in tumour metastasis and viral entry to cells, and therefore targeting these proteins may have other important applications.

Assay, reagents and screening readiness of the target

Our goal is to develop a reversible selective ERp57 inhibitor. To address this, we have developed a high throughput screening assay that has been used in a pilot study, screened against recombinant ERp57 that was produced in-house. From a panel of 3641 compounds 17 were found inhibit ERp57 activity. Only 1 compound satisfied our confirmatory criteria and showed strong selectivity over other platelet thiol isomerases, although this exhibited a relatively high IC_{50} . The compound was able to inhibit platelet aggregation and adhesion as well as diminish thrombus formation *in vitro*. Our pilot study suggests that our assay, which was used in 1536 well plate format is appropriate for application for an extensive screen, with a secondary fluorescence-based assay and appropriate biological assays established.

Additional non-confidential information:

The discovery of ERp57 as a regulator of haemostasis and thrombosis was made in the Gibbins group in Reading, and has subsequently been validated using transgenic ERp57 deficient mice by other researchers. The screen used in our pilot study was adapted by Dr Kennedy (University of Western New England) from existing assays of reductase activity and the screen was performed at the Longwood Screening Facility, Harvard University. Specificity analysis and biological activity testing was performed in the Gibbins laboratory in Reading.

