

July 17, 2017  
Paul DaSilva Jardine  
Vascumab, LLC  
23 Business Park Drive  
Branford, CT 06405

Br. 2

Scott Wilson  
Health Physicist  
NRC Region I  
2100 Renaissance Blvd, Ste 100  
King of Prussia, PA 19406

Mr. Wilson,

I am writing this letter to request that Margit MacDougall be added to our list of users of approved radioactive materials ( $^3\text{H}$ ,  $^{14}\text{C}$ ,  $^{33}\text{P}$ ,  $^{125}\text{I}$ ). I have attached Margit's CV. You will see that she has experience with the use of radioisotopes that we are currently approved for.

Our license number is 06-35389-01 and our docket number is 03039010.

Thank You.



Paul DaSilva Jardine  
President, Vascumab, LLC

600168

NRC/RGN MATERIALS-002

## MARGIT MACDOUGALL

### SUMMARY

Dedicated and productive research scientist with more than 20 years experience in the pharmaceutical industry, specializing in *in vitro* and *ex vivo* assay development and execution. Extensive drug discovery experience for both small molecule and Biotherapeutic drug candidates targeting Cardiovascular and Metabolic disease indications. Proven ability to develop critical assays and prosecute targets to meet and exceed deliverable goals and timelines. Effective team contributor with strong analytical abilities and sound decision making.

### EXPERIENCE

VASCUMAB, Inc., Branford, CT

**Principle Research Scientist, Pharmacology**

2017 – present

BOEHRINGER INGELHEIM PHARMACEUTICALS, Inc., Ridgefield, CT

**CardioMetabolic Disease Research**

2014 - 2017

**Biotherapeutics, Pharmacology Group**

2011 – 2013

**Scientist IV**

- Served as the *in vitro* Project Discipline Leader for an innovative vascular protection kidney target providing both strategic and assay support for rapid advancement of the project
- Developed blocking ELISA and functional assays in endothelial cells to support triage strategy for glomerular filtration barrier target
- Optimized and validated enzymatic functional assay to enable screening of candidate antibodies for a renal fibrosis target
- Developed and executed cellular functional assays to support lead identification efforts for high profile Atherosclerosis target
- Utilized high content imaging to measure internalization and determine binding mode of preclinical drug candidate
- Generated functional cell lines utilizing retroviral infection method to support lead generation efforts for Biotherapeutic targets
- Represent department on cross functional teams, collaborate effectively, and communicate efforts and results within project context to department and project teams

PFIZER, Inc., Groton, CT

2007 – 2011

**Cardiovascular and Metabolic Diseases, Diabetes Best in Class Unit**

**Senior Scientist**

- Primary islet biologist for multiple diabetes drug discovery programs, responsible for developmental of islet technology platform and design of program strategy for evaluation of insulin secretion and islet function
- Supported identification of clinical candidate compounds through screening in INS-1 cells and isolated islets
- Utilized the perfusion technique to characterize differences in glucose thresholds for insulin secretion in rat, monkey and human islets and modulation of thresholds with key compounds
- Established platform in Type 2 Diabetic islets to evaluate recovery of function and glucose sensitivity with benchmark and proprietary compounds
- Coordinated a cross functional team to execute a polyomic study (metabonomics, proteomics, genomics) to characterize the metabolic effects of glucagon receptor ablation
- Developed a primary hepatocyte assay to look at changes in malonyl CoA levels and evaluate active uptake through organic anion transporting polypeptides
- Primary contributor of data and author of study reports for two IND filings, programs progressed to Phase 2 clinical development

**BAYER HEALTHCARE, West Haven, CT**  
**Department of Protein Therapeutics, Oncology**  
**Scientist/Senior Investigator I**

2006 – 2007

- Established apoptosis assays utilizing flow cytometry (FACS) to evaluate potential toxins for peptide conjugation and targeted chemotherapeutic
- Developed ELISAs and performed cell proliferation assays for peptide target
- Author of provisional patent for peptide therapeutic
- Project leader for new Cancer protein therapeutic, including organization of kickoff meeting, development of screening cascade, FTO and competition analysis

**BAYER HEALTHCARE, West Haven, CT**  
**Department of Metabolic Disorders Research**  
**Scientist**  
**Senior Associate Research Scientist**  
**Associate Research Scientist**

2000 – 2006

1995 – 2000

1992 – 1995

- Performed diabetes target identification, development of primary and secondary screening assays, evaluation of chemical matter, and assay support for pre-clinical to clinical candidates. Experience leading assay development and biology target prosecution teams
- Designed, developed, and validated ELISA methodology to support PK analysis of pre-clinical and clinical peptide programs for both Diabetes and Obesity. Projects included GLP-1 agonist/glucagon antagonist, VPAC2 receptor and NPY2 receptor
- Coordinated assay development between Bayer research sites, prepared documents and served as a liaison with an external CRO for effective assay transfer and validation
- Effective cross functional interactions with members of chemistry, pharmacokinetics, product development, research technologies and toxicology toward advancement of diabetes projects
- Established methods for measuring apoptosis in beta cell lines and utilized them for validation of benchmark compounds and evaluation of clinical candidates
- Served as Diabetes small molecule project coordinator for multiple targets, including PDEs 10 and 11
- Performed two critical assays to identify glucagon antagonist small molecule which reached phase II clinical development
- Performed in vivo experiments in mice and rats to evaluate compounds for cytochrome P450 induction

**EDUCATION**

**MS Cellular and Molecular Biology** University of New Haven, West Haven, CT

**BA Psychobiology** Hamilton College, Clinton, NY

**TECHNICAL SKILLS**

**Cell Biology**

- Mammalian cell culture
- Chemotaxis
- Calcium flux (FLIPR)
- Flow cytometry (FACS)
- High content imaging
- Stable and transient transfections and infections
- Single cell cloning
- Insulin and glucagon secretion
- cAMP/cGMP production
- Cellular proliferation
- Apoptosis (annexin V, caspase, TUNEL)

**Biochemistry**

- Ligand receptor binding assays
- Enzymatic activity assays
- RIA
- PDE activity assays
- SDS-PAGE
- Western blotting
- IHC
- Biorad/Lowry protein assays
- Cytochrome P450 measurements

**Immunology**

- ELISA development and validation
- Monoclonal and polyclonal antibody production
- Antibody titer assays
- Antibody neutralization assays

**Molecular Biology**

- DNA and RNA isolation
- TaqMan
- Northern and southern blotting
- PCR

### Ex Vivo/In Vivo

- Isolation and ex vivo secretion assays in rat islets
- Perfusion of rodent, monkey and human islets
- Isolation and primary culturing of rat hepatocytes
- Analyses of serum and plasma samples
- Small animal handling, dosing and necropsy

### RADIOACTIVITY USE EXPERIENCE

- University of Rochester, 1988 – 1992
  - $^{125}\text{I}$ ,  $^3\text{H}$ ,  $^{35}\text{S}$ -methionine
  - Pulse chase experiments, other assays with low micro curie levels of radioactivity
  - Completed annual radiation safety user training
- Bayer Healthcare, 1992 – 2007
  - $^{125}\text{I}$ ,  $^3\text{H}$ ,  $^{32}\text{P}$ ,  $^{14}\text{C}$
  - Radioimmunoassays for insulin and glucagon, other assays with low micro curie levels of radioactivity
  - Completed annual radiation safety user training
- Pfizer, Inc., 2007 – 2011
  - $^{125}\text{I}$ ,  $^3\text{H}$
  - Low micro curie level use of radioactivity
  - Completed annual radiation safety user training

### COMPUTER SKILLS

- Microsoft Word
- Microsoft Excel
- Microsoft PowerPoint
- GraphPad Prism
- Microsoft FrontPage
- SOFTmax Pro

### AWARDS

- Pfizer Individual Performance Award for Above and Beyond contributions (2011)
- Bayer Big Team Awards: Peptide Assay Development (2003), Apoptosis (2006)
- Bayer Science and Technology Award: Dual Acting Peptide for Diabetes (2002)
- Special recognition awards for Innovation, Leadership, Delivering Results, Above and Beyond contributions, Champion for Change
- Multiple On the Spot awards awarded for extra effort to advance project goals
- Outstanding performance ranking (2005) and multiple exceeded expectations

### PUBLICATIONS

Pfefferkorn JA, Tu M, Filipinski KJ, Guzman-Perez A, Bian J, Aspnes GE, Sammons MF, Song W, Li JC, Jones CS, Patel L, Rasmusson T, Zeng D, Karki K, Hamilton M, Hank R, Atkinson K, Litchfield J, Aiello R, Baker L, Barucci N, Bourassa P, Bourbonais F, D'Aquila T, Derksen DR, **MacDougall M**, Robertson A  
"The design and synthesis of indazole and pyrazolopyridine based glucokinase activators for the treatment of Type 2 diabetes mellitus" *Bioorg. Med. Chem. Lett.* 22 (2012) 7100-7105.

Pfefferkorn JA, Guzman-Perez A, Litchfield J, Aiello R, Treadway JL, Petterson J, Minich ML, Filipinski KJ, Jones CS, Tu M, Aspnes GE, Risley H, Bian J, Stevens BD, Bourassa P, D'Aquila T, Baker L, Barucci N, Robertson AS, Bourbonais F, Derksen DR, **MacDougall M**, Cabrera O, Chen J, Lapworth AL, Landro J, Zavadoski WJ, Atkinson K, Haddish-Berhane N, Tan B, Yao L, Kosa RE, Varma MV, Feng B, Duignan DB, El-Kattan A, Murdande S, Liu S, Ammirati M, Knafels J, Dasilva-Jardine P, Sweet L, Liras S, Rolph T  
"Discovery of (S)-6-(3-cyclopentyl-2-(4-(trifluoromethyl)-1H-imidazol-1-yl)propanamido)nicotinic acid as a hepatoselective glucokinase activator clinical candidate for treating Type 2 diabetes mellitus" *J Med Chem.* (2012) Feb 9; 55(3) (2012) 3118-3133.

Pfefferkorn JA, Guzman-Perez A, Oates PJ, Litchfield J, Aspnes G, Basak A, Benbow J, Berliner M, Bian J, Choi C, Didiuk M, Filipski K, Hungerford WM, Karaki KK, Ling A, Li JC, Patel L, Tu M, Aiello R, Atkinson K, Barucci N, ~~Baile D~~, Bourassa P, Bourbonais F, Brodeur AM, Burbey R, Chen J, D'Aquila T, Derksen DR, Haddish-Berhane N, Huang C, Landro J, **MacDougall M**, Perregaux D, Petterson J, Robertson A, Treadway J, Liu S, Qiu X, Knafels J, Ammirati M, Song X, Dasilva-Jardine P, Liras S, Sweet L. "Designing Glucokinase Activators with Reduced Hypoglycemia Risk: Discovery of *N,N*-dimethyl-5-(2-methyl-6-((5-methylpyrazin-2-yl)-carbamoyl)benzofuran-4-yloxy)pyrimidine-2-carboxamide as a Clinical Candidate for the Treatment of Type 2 Diabetes Mellitus" *MedChemComm*. (2011) DOI: 10.1039/C1MD00116G.

Yang J, **MacDougall ML**, McDowell MT, Xi L, Wei R, Zavadoski WJ, Molloy MP, Baker JD, Kuhn M, Cabrera O, Treadway JL. "Polyomic Profiling Reveals Significant Metabolic Alterations in Glucagon Receptor (GCGR) Knockout Mice" *BMC Genomics* (2011) 12:281.

Wunderlich DA, **MacDougall M**, Mierz DV, Toth JG, Buckholz TM, Lumb KJ, Vasavada H. "Generation and characterization of a monoclonal IgG antibody to polyethylene glycol" *Hybridoma* (2007) 26 (3): 168-172.

Cantin LD, Magnuson S, Gunn D, Barucci N, Breuhaus M, Bullock W, Burke J, Claus T, Daly M, DeCarr L, Gore-Willse A, Hoover-Litty H, Kumarasinghe ES, Li Y, Liang SX, Livingston JN, Lowinger T, **MacDougall M**, Ogutu HO, Olague A, Ott-Morga R, Schoenleber R, Tersteegen A, Wickens P, Zhang Z, Zhu J, Zhu L, Sweet LJ. "PDE-10A inhibitors as insulin secretagogues" *Bioorg Med Chem Lett*. 17 (2007) 2869-2873.

Pan CQ, Buxton JM, Yung SL, Tom I, Yang L, Chen H, **MacDougall M**, Bell A, Claus TH, Clairmont KB, and Whelan JP. "Design of a long-acting peptide functioning as both a glucagon-like peptide-1 receptor agonist and a glucagon receptor antagonist" *J Biol Chem*. (2006) May 5; **281**(18):12506-15.

Yung SL, Dela Cruz F, Hamren S, Zhu J, Tsutsumi M, Bloom JW, Caudle M, Rocznik S, Todd T, Lemoine L, **MacDougall M**, Shanafelt AB, and Pan CQ. "Generation of highly selective VPAC2 receptor agonists by high throughput mutagenesis of vasoactive intestinal peptide and pituitary adenylate cyclase-activating peptide" *J Biol Chem*. (2003) Mar 21; **278**(12):10273-81.

Ladouceur GH, Cook JH, Hertzog DL, Jones HJ, Hundertmark T, Korpusik M, Lease TG, Livingston JN, **MacDougall M**, Osterhout MH, Phelan K, Romero RH, Schoen WR, Shao C, and Smith RA. "Integration of optimized substituent patterns to produce highly potent 4-aryl-pyridine glucagon receptor antagonists" *Bioorg Med Chem Lett*. (2002) Dec 2; **12**(23):3421-4.

Smith RA, Hertzog DL, Osterhout MH, Ladouceur GH, Korpusik M, Bobko MA, Jones HJ, Phelan K, Romero RH, Hundertmark T, **MacDougall ML**, Livingston JN, and Schoen WR. "Optimization of the 4-aryl group of 4-aryl-pyridine glucagon antagonists: development of an efficient, alternative synthesis" *Bioorg Med Chem Lett*. (2002) May 6; **12**(9):1303-6.

Ladouceur GH, Cook JH, Doherty EM, Schoen WR, **MacDougall ML**, and Livingston JN. "Discovery of 5-hydroxyalkyl-4-phenylpyridines as a new class of glucagon receptor antagonists" *Bioorg Med Chem Lett*. (2002) Feb 11; **12**(3):461-4.

Buggy J.J., Heurich R., **MacDougall M.**, Kelley K.A., Livingston J.N., Yoo-Warren H., and Rossomando A.J. "Role of the Glucagon Receptor COOH-Terminal Domain in Glucagon-Mediated Signaling and Receptor Internalization" *Diabetes* (1997), **46** (9), 1400-1404.

Buggy J, Rossomando A, **MacDougall M**, Mierz D, Wunderlich D, and Yoo-Warren H. "Human glucagon receptor monoclonal antibodies: antagonism of glucagon action and use in receptor characterization" *Horm Metab Res*. (1996) May; **28**(5):215-9.

Jackson T.K., Salhanick A.I., Elovson J., **Deichman M.**, and Amatruda J.M. "Insulin regulates apolipoprotein B turnover and phosphorylation in rat hepatocytes" *J. Clin. Invest.* (1990), **86**, 1746-1751.

Author of 16 Bayer internal reports

Author of 2 Pfizer internal study reports



ACKNOWLEDGEMENT - RECEIPT OF CORRESPONDENCE

Name and Address of Applicant and/or Licensee

Vascumab, LLC  
ATTN: Paul DaSilva Jardine, Owner and CEO  
23 Business Park Drive  
Branford, CT 06405

Date

July 18, 2017

License Number(s)

06-35389-01

Mail Control Number(s)

600168

Licensing and/or Technical Reviewer or Branch

Commercial, Industrial, R&D, & Academic Branch  
(Branch 2)

This is to acknowledge receipt of your:  Letter and/or  Application Dated: 07/17/2017

The initial processing, which included an administrative review, has been performed.

Amendment  Termination  New License  Renewal

There were no administrative omissions identified during our initial review.

This is to acknowledge receipt of your application for renewal of the material(s) license identified above. Your application is deemed timely filed, and accordingly, the license will not expire until final action has been taken by this office.

Your application for a new NRC license did not include your taxpayer identification number. Please complete and submit NRC Form 531, Request for Taxpayer Identification Number, located at the following link: <http://www.nrc.gov/reading-rm/doc-collections/forms/nrc531.pdf>  
Follow the instructions on the form for submission.

The following administrative omissions have been identified:

[Empty box for listing administrative omissions]

Your application has been assigned the above listed MAIL CONTROL NUMBER. When calling to inquire about this action, please refer to this control number. Your application has been forwarded to a technical reviewer. Please note that the technical review, which is normally completed within 180 days for a renewal application (90 days for all other requests), may identify additional omissions or require additional information. If you have any questions concerning the processing of your application, our contact information is listed below:

Region I  
U. S. Nuclear Regulatory Commission  
Division of Nuclear Materials Safety  
2100 Renaissance Boulevard, Suite 100  
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(610) 337-5398, or (610) 337-5239