BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: PASQUALINI, RENATA

eRA COMMONS USER NAME (credential, e.g., agency login): rpasqual

POSITION TITLE: Professor and Chief, Division of Cancer Biology, Dept of Radiation Oncology

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing,

include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of São Paulo, Brazil	BS	12/1986	Biological Sciences
University of São Paulo, Brazil	PhD	04/1990	Biochemistry
The Children's Hospital, Harvard University, Boston, MA	Postdoctoral Fellow	05/1991	Cell Biology
Dana Farber Cancer Institute, Boston, MA	Postdoctoral Fellow	12/1994	Cell Biology, Biochemistry
The Burnham Institute, La Jolla, CA	Fellow	12/1996	Cell Biology, Biochemistry

A. Personal Statement

Currently, I am a Professor of Radiation Oncology and Chief of the Division of Cancer Biology at Rutgers New Jersey Medical School and Rutgers Cancer Institute of New Jersey. In 1999, I established a joint laboratory with Wadih Arap, MD, PhD, at the University of Texas M.D. Anderson Cancer Center, where we stayed until 2013, when we relocated to UNMCC. I am an internationally recognized expert in vascular biology, metastasis, and angiogenesis. I originally co-developed in vivo phage display and have been recognized for my contribution to identifying organ- and tumor-specific ligands to target vascular receptors. Our group has been working with all aspects of phage display technology for almost 25 years and we have published extensively in this area. The central working hypothesis of our research program is that differential protein expression in the human vascular endothelium, associated with normal or diseased tissues, offers the potential for developing novel diagnostic, imaging, and therapeutic strategies. Our program uses peptide- and antibody-based combinatorial library selection to discover, validate, and exploit the vascular biochemical diversity of endothelial cell surfaces towards identifying new vascular targeted agents for the treatment of diseases including cancer, obesity, retinopathy, and more. Our team has a long track record of productive scientific discovery related to cancer biology and translational medicine that includes 230 joint publications in high-quality journals, 23 issued US patents, and a drug development pipeline that includes an anti-cancer peptide-drug conjugate with specific affinity for bone marrow metastases from prostate cancer and an anti-obesity agent, both of which were successfully evaluated in Phase I studies, two other drugs are in the pre-IND stage, and several others in pre-clinical laboratory phase. Long-term, the broader vision of our research is a large-scale mapping of receptors in human vasculature towards a new ligand-directed pharmacology. Accordingly, these efforts align with my membership in the Cancer Pharmacology Program at CINJ.

Ongoing and recently completed projects that I would like to highlight include:

R01CA226537

PI: Arap, Pasqualini, Cristini, Brinker

08/01/2018 - 07/23/2023

A Targeted Nanomedicine Prototype against Enzalutamide-resistant Prostate Cancer

R01CA218853

PI: Pasqualini

06/04/2018 - 05/31/2023

Functional Targeting of the Tyrosine Kinase EphA5 in Radiation-resistant Lung Cancer

R01CA240516

PI: Pasqualini, Arap, Libutti 03/15/2020 - 02/28/2025

Designing a Transcriptome-Based, Targeted Theranostic Platform for Prostate Cancer

Citations of recent programmatic milestones:

- Burley SK, Arap W, Pasqualini R. Predicting Proteome-Scale Protein Structure with Artificial Intelligence. N Engl J Med. 2021 Dec 2;385(23):2191-2194. PMID: 34874637
- Staquicini FI, Hajitou A, Driessen WH, Proneth B, Cardó-Vila M, Staquicini DI, Markosian C, Hoh M, Cortez M, Hooda-Nehra A, Jaloudi M, Silva IT, Buttura J, Nunes DN, Dias-Neto E, Eckhardt B, Ruiz-Ramírez J, Dogra P, Wang Z, Cristini V, Trepel M, Anderson R, Sidman RL, Gelovani JG, Cristofanilli M, Hortobagyi GN, Bhujwalla ZM, Burley SK, Arap W, Pasqualini R. Targeting a cell surface vitamin D receptor on tumorassociated macrophages in triple-negative breast cancer. Elife. 2021 Jun 1;10:e65145. PMID: 34060472; PMCID: PMC8169110
- Staquicini DI, Tang FHF, Markosian C, Yao VJ, Staquicini FI, Dodero-Rojas E, Contessoto VG, Davis D, O'Brien P, Habib N, Smith TL, Bruiners N, Sidman RL, Gennaro ML, Lattime EC, Libutti SK, Whitford PC, Burley SK, Onuchic JN, Arap W, Pasqualini R. Design and proof of concept for targeted phage-based COVID-19 vaccination strategies with a streamlined cold-free supply chain. Proc Natl Acad Sci USA. 2021 Jul 27;118(30):e2105739118. PMID: 34234013; PMCID: PMC8325333
- 4. Staquicini DI, Barbu EM, Zemans RL, Dray BK, Staquicini FI, Dogra P, Cardó-Vila M, Miranti CK, Baze WB, Villa LL, Kalil J, Sharma G, Prossnitz ER, Wang Z, Cristini V, Sidman RL, Berman AR, Panettieri Jr RA, Tuder RM, **Pasqualini R**, Arap W. Targeted phage display-based pulmonary vaccination in mice and non-human primates. Med (NY). 2021 Mar 12;2(3):321-342. PMID: 33870243; PMCID: PMC8049167.

B. Positions, Scientific Appointments, and Honors

Positions

FUSILIUIIS	
2018-Present	Professor, Department of Radiation Oncology and Chief, Division of Cancer Biology, Rutgers
	New Jersey Medical School, Rutgers Cancer Institute of New Jersey, Newark, NJ
2013-2017	Maralyn S. Budke Professor of Medicine, Associate Director for Translational Research,
	Chief, Division of Molecular Medicine, University of New Mexico Comprehensive Cancer
	Center, Albuquerque, NM
2003-2013	Helen Buchanan & Stanley Seeger Professor of Medicine and Experimental Diagnostic
	Imaging, University of Texas MD Anderson Cancer Center, Houston, TX
1999-2003	Associate Professor, UT MD Anderson Cancer Center, Houston, TX
1997-1999	Assistant Professor, The Burnham Institute, La Jolla, CA

Scientific Appointments

Ocientine Appointments
2023-present Research in Progress Evaluation Committee, CINJ, Rutgers University
2022-present Member, Scientific Advisory Board, BZKF (Bavarian Cancer Research Center), Germany.
2021-present eLife Reviewing Editor, Medicine and Cancer Biology

2021 Chair, NIH PAR Panel: Innovative Research in Cancer Nanotechnology; Member, eLife Board of Reviewing Editors for Medicine

2020-present Member, REACH (Research Evaluation and Commercialization Hubs) Executive Committee
2020 Chair, NIGMS MIRA ESI Study Section; Reviewer, NIH Director's DP5 Early Independence
Award

2019 Member, NIH, Tumor Microenvironment Study Section; Member, AACR Neuroendocrine Tumor Research Grants Scientific Review Committee

2018-present Research Leadership Council, CINJ, Rutgers University

2018-present Co-Chair, CETI (Committee for Expediting Translational Initiatives), CINJ, Rutgers University
 Member, NIH, Nanotechnology Study Section; Member, NIH, Stimulating Peripheral Activity to Relieve Conditions (SPARC) Review Committee

2017 Reviewer, French National Cancer Institute; Member, Stanford Patent Peer Review Project; Nomination Committee, Japan Prize Foundation

2016-2017 Chair, American Association for Cancer Research, Neuroendocrine Tumor Research Foundation, AACR Grant Scientific Review Committee

2016	Chair, Bioengineering Sciences and Technologies IRG, BST-X(02) M review panel;
0045	Reviewer, Australian Academy of Health & Medical Sciences, Academy of Finland
2015	Member, NIH Vascular Cell and Molecular Biology and Nanotechnology Study Sections;
0044	Chair, DoD Innovator Award Study Section
2014	Chair, DOD BCRP Nanotechnology Review Panel; Member, Methusalen Angiogenesis
	Center Site Visit, Belgium
2013	Member, Advisory Board, Common Fund Protein Capture Initiative
2012	Reviewer, American Cancer Society; NCATS Review Branch, NIH Therapeutics Discovery
	Review
2010-2012	Chair, Gene and Drug Delivery (GDD) study section
2010	Member, Chair, DOD BCRP, Era of Hope Scholar Award Review; GDD Study Section, NIH;
	Reviewer, The C. Hilton Foundation; Agence Nationale de la Recherche
2009	Member, GDD Study Section, NIH; Concept Awards, DOD BCRP Review Panel; Ministero
	dell'Istruzione, dell'Università e della Ricerca; Italian Association for Cancer Research
	(AIRC); Chair, DOD BCRP Era of Hope Scholar Award; NIH Challenge Grants; European
	Res Council Executive Agency Advanced Grant; Reviewer, S. G. Komen Foundation; QED
	Program; American Inst for Biol Sci
2008	Member, Review Board, US-Israel Binational Science Foundation, The Foundation for
	Science and Technol UK, NIH Gene and Drug Delivery Study Section, Organizing
	Committee, Am Soc Mol Imaging
2007	Member, Organizing Committee, Am Soc Mol Imaging; Ad Hoc Member, Gene and Drug
	Delivery Study Section (NCI); Organizing Committee, iSBT Review panel, IMPACT, DOD
	BCRP Review Panel

<u>Honors</u>

2023	Torian Barineau Fund Award
2021-2023	The Levy-Longenbaugh Foundation Award
2012	The Carcinoid Foundation Investigator Award, AACR
2011	Lombroso Achievement Award, Weizmann Institute of Science
2010	Distinguished Women in Science, BioHouston
2010	Prostate Cancer Foundation Creativity Award
2009	Edith and Peter O'Donnell Award, Academy of Medicine, Engineering, and Science of Texas
2009	Potu N. Rao Award for Excellence in Basic Science, Division of Cancer Medicine, MD
	Anderson Cancer Center
2007	The Top 400 Inventors for 99% of patents filed since 1946
2006	Living Legend Faculty Achievement Award, MD Anderson Cancer Center
2006	Fellows of the MD Anderson Research Trust Award
2006	Marcus Foundation Award
2000-2020	The Gillson Longenbaugh Foundation Award

C. Contributions to Science

- 1. By combining the transduction capability of adeno-associated virus with the cell targeting capabilities of phage into a hybrid vector termed AAVP, we showed targeted-AAVP is able to systemically deliver genes to tumor vasculature for non-invasive imaging and/or tumor growth inhibition in mouse models including glioblastoma and prostate, breast, and neuroendocrine tumors. Two US patents (9,827,327 and 8,470,528) have been issued for AAVP compositions and their use in oncology applications.
 - a. Hajitou A, Trepel M, Lilley CE, Soghomonyan S, Alauddin MM, Marini FC 3rd, Restel BH, Ozawa MG, Moya CA, Rangel R, Sun Y, Zaoui K, Schmidt M, von Kalle C, Weitzman MD, Gelovani JG, Pasqualini R, Arap W. A hybrid vector for ligand-directed tumor targeting and molecular imaging. Cell. 2006 Apr 21;125(2):385-98. PMID: 16630824.
 - b. Ferrara F, Staquicini DI, Driessen WHP, D'Angelo S, Dobroff AS, Barry M, Lomo LC, Staquicini FI, Cardó-Vila M, Soghomonyan S, Alauddin MM, Flores LG 2nd, Arap MA, Lauer RC, Mathew P, Efstathiou E, Aparicio AM, Troncoso P, Navone NM, Logothetis CJ, Marchiò S, Gelovani JG, Sidman RL, **Pasqualini R**, Arap W. Targeted molecular-genetic imaging and ligand-directed therapy in aggressive variant prostate cancer. Proc Natl Acad Sci USA. 2016 Nov 8;113(45):12786-91. PMID: 27791181;

- PMCID: PMC5111687
- c. Dobroff AS, D'Angelo S, Eckhardt BL, Ferrara F, Staquicini DI, Cardó-Vila M, Staquicini FI, Nunes DN, Kim K, Driessen WH, Hajitou A, Lomo LC, Barry M, Krishnamurthy S, Sahin A, Woodward WA, Prossnitz ER, Anderson RL, Dias-Neto E, Brown-Glaberman UA, Royce ME, Ueno NT, Cristofanilli M, Hortobagyi GN, Marchiò S, Gelovani JG, Sidman RL, Arap W, Pasqualini R. Towards a transcriptome-based theranostic platform for unfavorable breast cancer phenotypes. Proc Natl Acad Sci USA. 2016 Nov 8;113(45):12780-5. PMID: 27791177; PMCID: PMC5111698.
- d. Staquicini FI, Smith TL, Tang FHF, Gelovani JG, Giordano RJ, Libutti SK, Sidman RL, Cavenee WK, Arap W, **Pasqualini R**. Targeted AAVP-based therapy in a mouse model of human glioblastoma: a comparison of cytotoxic versus suicide gene delivery strategies. Cancer Gene Ther. 2020 May;27(5):301-10. PMID: 31130731; PMCID: PMC6879804
- 2. End-of-life patients and their families who participated in a carefully designed and implemented study protocol provided a unique opportunity to identify novel zip codes. From this human study, we developed a peptide that specifically targeted interleukin-11 receptor alpha, which led to our first investigational new drug (IND), bone-metastasis targeting peptidomimetic against IL-11R (BMTP-11). Treatment of castrate-resistant metastatic prostate cancer patients verified peptide localization to bone marrow tumors and BMTP-11-induced apoptosis at multiple dose levels in all patients. IL-11R is also a viable marker for other tumor types, including osteosarcoma and lung cancers. Two US patents (7,671,010 and 8,507,445) have been issued to protect BMTP-11 and its use in oncology applications.
 - a. Arap W, Kolonin MG, Trepel M, Lahdenranta J, Cardó-Vila M, Giordano RJ, Mintz PJ, Ardelt PU, Yao VJ, Vidal CI, Chen L, Flamm A, Valtanen H, Weavind LM, Hicks ME, Pollock RE, Botz GH, Bucana CD, Koivunen E, Cahill D, Troncoso P, Baggerly KA, Pentz RD, Do KA, Logothetis CJ, Pasqualini R. Steps toward mapping the human vasculature by phage display. Nat Med. 2002 Feb;8(2):121-7. PMID: 11821895.
 - b. Staquicini FI, Cardó-Vila M, Kolonin MG, Trepel M, Edwards JK, Nunes DN, Sergeeva A, Efstathiou E, Sun J, Almeida NF, Tu SM, Botz GH, Wallace MJ, O'Connell DJ, Krajewski S, Gershenwald JE, Molldrem JJ, Flamm AL, Koivunen E, Pentz RD, Dias-Neto E, Setubal JC, Cahill DJ, Troncoso P, Do KA, Logothetis CJ, Sidman RL, Pasqualini R, Arap W. Vascular ligand-receptor mapping by direct combinatorial selection in cancer patients. Proc Natl Acad Sci USA. 2011 Nov 15;108(46):18637-42. PMID: 22049339; PMCID: PMC3219136.
 - c. Pasqualini R, Millikan RE, Christianson DR, Cardó-Vila M, Driessen WH, Giordano RJ, Hajitou A, Hoang AG, Wen S, Barnhart KF, Baze WB, Marcott VD, Hawke DH, Do KA, Navone NM, Efstathiou E, Troncoso P, Lobb RR, Logothetis CJ, Arap W. Targeting the interleukin-11 receptor α in metastatic prostate cancer: A first-in-man study. Cancer. 2015 Jul 15;121(14):2411-21. PMID: 25832466; PMCID: PMC4490036.
 - d. Lewis VO, Devarajan E, Cardó-Vila M, Thomas DG, Kleinerman ES, Marchiò S, Sidman RL, Pasqualini R, Arap W. BMTP-11 is active in preclinical models of human osteosarcoma and a candidate targeted drug for clinical translation. Proc Natl Acad Sci USA. 2017 Jul 25;114(30):8065-70. PMID: 28698375; PMCID: PMC5544306.
- 3. Use of combinatorial peptide libraries displayed on phage has identified novel, clinically relevant ligand-receptor pairs, termed 'zip-codes', for selective targeting of endothelial cells, perivascular cells, extracellular matrix, and tumor cells. Twenty-nine US patents have been issued for my pioneering efforts describing in vivo phage display and our later efforts to validate molecular zip-codes. These findings are currently being translated into clinical applications.
 - a. **Pasqualini R**, Ruoslahti E. Organ targeting in vivo using phage display peptide libraries. Nature. 1996 Mar 28;380(6572):364-6. PMID: 8598934.
 - b. Kolonin MG, Sergeeva A, Staquicini DI, Smith TL, Tarleton CA, Molldrem JJ, Sidman RL, Marchiò S, Pasqualini R, Arap W. Interaction between Tumor Cell Surface Receptor RAGE and Proteinase 3 Mediates Prostate Cancer Metastasis to Bone. Cancer Res. 2017 Jun 15;77(12):3144-3150. PMID: 28428279; PMCID: PMC5858698.
 - c. Staquicini DI, Barbu EM, Zemans RL, Dray BK, Staquicini FI, Dogra P, Cardó-Vila M, Miranti CK, Baze WB, Villa LL, Kalil J, Sharma G, Prossnitz ER, Wang Z, Cristini V, Sidman RL, Berman AR, Panettieri Jr RA, Tuder RM, **Pasqualini R**, Arap W. Targeted phage display-based pulmonary vaccination in mice and non-human primates. Med. 2021 Mar 12; 2(3):321-42.
 - d. Staquicini FI, Hajitou A, Driessen WH, Proneth B, Cardó-Vila M, Staquicini DI, Markosian C, Hoh M, Cortez M, Hooda-Nehra A, Jaloudi M, Silva IT, Buttura J, Nunes D, Dias-Neto E, Eckhardt B, Ruiz-

- Ramírez J, Dogra P, Wang Z, Cristini V, Trepel M, Anderson R, Sidman RL, Gelovani JG, Cristofanilli M, Hortobagy G, Bhujwalla ZM, Burley S, Arap W, **Pasqualini R**. Targeting a cell surface vitamin D receptor on tumor-associated macrophages in triple-negative breast cancer. Elife. 2021 Jun 1;10:e65145. PMID: 34060472; PMCID: PMC8169110.
- 4. We have been also developing a nanotechnology program based on a synaphic approach. To circumvent the enhanced permeability retention effect, targeting nanocarriers to tumors relies on using peptide ligands or antibody moieties that bind specifically to tumor-specific receptors or epitopes, respectively, to deliver their therapeutic payload in either phage-based hydrogels or conjugated to loaded nanoparticles. Nanocarrier payloads consist of cytotoxins, apoptotic peptides, siRNAs or imaging agents. We have also reported a levitated three-dimensional tissue culture methodology with magnetized phage-based hydrogels that closely recapitulates in vivo protein expression and may be more feasible for long-term multicellular studies. Three US patents have been issued for this patterning cells with magnetic guidance in hydrogel platforms.
 - a. Yao VJ, D'Angelo S, Butler KS, Theron C, Smith TL, Marchiò S, Gelovani JG, Sidman RL, Dobroff AS, Brinker CJ, Bradbury AR, Arap W, **Pasqualini R**. Ligand-targeted theranostic nanomedicines against cancer. J Control Release. 2016 Oct 28;240:267-286. PubMed PMID: 26772878.
 - b. Hosoya H, Dobroff AS, Driessen WH, Cristini V, Brinker LM, Staquicini FI, Cardó-Vila M, D'Angelo S, Ferrara F, Proneth B, Lin YS, Dunphy DR, Dogra P, Melancon MP, Stafford RJ, Miyazono K, Gelovani JG, Kataoka K, Brinker CJ, Sidman RL, Arap W, Pasqualini R. Integrated nanotechnology platform for tumor-targeted multimodal imaging and therapeutic cargo release. Proc Natl Acad Sci U S A. 2016 Feb 16;113(7):1877-82. PubMed PMID: 26839407; PubMed Central PMCID: PMC4763738.
 - c. Souza GR, Molina JR, Raphael RM, Ozawa MG, Stark DJ, Levin CS, Bronk LF, Ananta JS, Mandelin J, Georgescu MM, Bankson JA, Gelovani JG, Killian TC, Arap W, **Pasqualini R**. Three-dimensional tissue culture based on magnetic cell levitation. Nat Nanotechnol. 2010 Apr;5(4):291-6. PMID: 20228788; PMCID: PMC4487889
 - d. Souza GR, Christianson DR, Staquicini FI, Ozawa MG, Snyder EY, Sidman RL, Miller JH, Arap W, **Pasqualini R**. Networks of gold nanoparticles and bacteriophage as biological sensors and cell-targeting agents. Proc Natl Acad Sci U S A. 2006 Jan 31;103(5):1215-20. PubMed PMID: 16434473; PubMed Central PMCID: PMC1346765.
- 5. We have further engineered the phage genome to divergent goals: a) direct administration of a phage displaying a peptide directing the particle across the air-blood barrier in the lungs and into the circulation for immunization strategies, b) capsid modifications allow the particles to avoid physiologic barriers in the circulation and increase transduction efficiency, and c,d) phage that express the penetration peptide sequence on the major pVIII coat protein were designed to allow receptor independent cell entry. By expressing short peptides on the minor pIII coat protein, internalized phage (iPhage) peptide libraries can be screened to reveal cell surface proteins present on intracellular organelles or proteins within the cytoplasm. There are two pending US (and additional international) patent applications to protect engineered phage vaccines against Sars-CoV-2 and other pathogens.
 - a. Staquicini DI, Tang FHF, Markosian C, Yao VJ, Staquicini FI, Dodero-Rojas E, Contessoto VG, Davis D, O'Brien P, Habib N, Smith TL, Bruiners N, Sidman RL, Gennaro ML, Lattime EC, Libutti SK, Whitford PC, Burley SK, Onuchic JN, Arap W, Pasqualini R. Design and proof-of-concept for targeted phage-based COVID-19 vaccination strategies with a streamlined cold-free supply chain. Proc Natl Acad Sci USA. 2021 Jul 27;118(30):e2105739118. PMID: 34234013; PMCID: PMC8325333
 - b. Suwan K, Yata T, Waramit S, Przystal JM, Stoneham CA, Bentayebi K, Asavarut P, Chongchai A, Pothachareon P, Lee K-Y, Topanurak S, Smith TL, Gelovani JG, Sidman RL, **Pasqualini R**, Arap W, Hajitou A. Next-generation of targeted AAVP vectors for systemic transgene delivery against cancer, Proc Natl Acad Sci USA, 2019 Aug 2. pii: 201906653. doi: 10.1073/pnas.1906653116. PMID: 31375630.
 - c. Rangel R, Guzman-Rojas L, le Roux LG, Staquicini FI, Hosoya H, Barbu EM, Ozawa MG, Nie J, Dunner K Jr, Langley RR, Sage EH, Koivunen E, Gelovani JG, Lobb RR, Sidman RL, **Pasqualini R**, Arap W. Combinatorial targeting and discovery of ligand-receptors in organelles of mammalian cells. Nat Commun. 2012 Apr 17;3:788. PMID: 22510693; PMCID: PMC3337985.
 - d. Staquicini DI, Rangel R, Guzman-Rojas L, Staquicini FI, Dobroff AS, Tarleton CA, Ozbun MA, Kolonin MG, Gelovani JG, Marchiò S, Sidman RL, Hajjar KA, Arap W, **Pasqualini R**. Intracellular targeting of annexin A2 inhibits tumor cell adhesion, migration, and in vivo grafting. Sci Rep. 2017 Jun 26;7(1):4243. PMID: 28652618; PMCID: PMC5484684.