BIOGRAPHICAL SKETCH

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NAME: ARAP, WADIH

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POSITION TITLE: Professor and Chief, Division of Hematology/Oncology, Rutgers Cancer Institute of New Jersey at University Hospital

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 Medical School, Brazil	MD	12/1983	Medicine
University of São Paulo Medical School, Brazil	Resident	12/1986	Internal Medicine
Memorial Sloan-Kettering Cancer Center, New York, NY	Resident	07/1991	Medical Oncology, Hematology
Stanford University, Palo Alto, CA	PhD	12/1996	Cancer Biology
The Burnham Institute, La Jolla, CA	Fellow	10/1998	Cell Biology, Biochemistry

A. Personal Statement

I am Director of the Rutgers Cancer Institute of New Jersey at University Hospital in Newark, NJ, Co-Program Leader of the Clinical Investigations and Precision Therapeutics Research Program at Rutgers Cancer Institute, Professor of Medicine, Chief of the Division of Hematology/Oncology, and an attending physician at Rutgers New Jersey Medical School. As Program Co-Leader, I work to carefully select and mentor Program Members, and foster an interactive and cancer-focused environment that leads to impactful science. As a physician-scientist, my laboratory-based research focuses on the translation of discoveries into clinical applications. Dr. Renata Pasqualini and I have a long-standing collaboration and have led a joint laboratory (please note that we are also husband-and-wife) starting at The University of Texas MD Anderson Cancer Center in October 1999, and currently at Rutgers Cancer Institute of New Jersey (CINJ) in Newark, NJ. We have jointly published more than 230 peer-reviewed manuscripts, and, with very rare exceptions, such publications are a team science effort. Our efforts have been based on the scientific premise that differential protein expression in disease tissues will enable a new vascular-targeted pharmacology. Conceptually, molecules differentially expressed and accessible to circulating synthetic or native ligands--either among organs or between damaged and normal tissues--present attractive therapy targets. The molecular diversity of receptors in the human vasculature remains largely unexplored. Using *in vivo*, *in vitro* and *ex vivo* phage display, we identified several peptides as robust tumor targeting entities that bind specifically to the angiogenic vasculature. The combinatorial discovery of functional protein-protein interactions in the context of human disease is a versatile platform to effectively exploit, especially by integrating genomic analyses and analytical high-throughput technology. Our targeting technologies have led to the design and engineering of unique delivery vehicles based on targeted peptides or antibodies that will be optimized to deliver therapeutic agents to treat disease in patients. In addition to this productive research program, I have a longstanding clinical practice where I specialize in genitourinary medical oncology, prostate cancer specifically, and a successful history of translating benchtop discoveries to targeted drug candidates for clinical applications, having successfully taken two drug candidates from the bench to phase I clinical trials.

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

R01CA240516
PI: Pasqualini, Arap, Libutti
03/15/2020 - 02/28/2025
Designing a Transcriptome-Based, Targeted Theranostic Platform for Prostate Cancer

Relevant programmatic citations:

1. 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
2. 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.
3. **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.
4. 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. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2020-present	Program Co-Leader, Clinical Investigations and Precision Therapeutics Research Program, CINJ
2018-present	Director, Cancer Institute of New Jersey at University Hospital, Professor of Medicine, New Jersey Medical School, Attending Physician, Chief of Hematology/Oncology
2013-2017	Victor and Ruby Hansen Surface Professor of Medicine, Attending Physician, Division of Hematology/Oncology, Deputy Director, University of New Mexico Comprehensive Cancer Center, Albuquerque, NM
2010	Member, NIH, Board of Scientific Advisors
2009	Co-chair, Radiation Oncology Branch Site Visit
2008	Co-chair, Experimental Transplantation and Immunology Branch Site
2007	Member, DOD PCRP Integration Panel
2006-2013	Deputy Chairman, David H. Koch Center, The University of Texas M. D. Anderson Cancer Center, Houston, TX
2006-2011	Member, NIH – NCI Board of Scientific Counselors
2004-2006	Member, Study Section Review Committees for Clinical Translational Research Projects
2004	Member, Experimental Transplantation and Immunology Branch Site Visit
2003-2013	Attending Physician, Stringer Professor of Medicine & Experimental Diagnostic Imaging, The University of Texas MD Anderson Cancer Center, Houston, TX
2003-2005	Member, Technology Review Committee, MDACC; NCI Review R33 “IMAT”; Vienna Science and Technology Fund, Hong Kong SAR Government
2000-2001	Member, Susan G. Komen Breast Cancer Foundation, NIH Rapid Access to Intervention Development Program, Prostate Cancer SPORE Study Section, Health Research Board, Ireland, Extramural Advisory Board, Vascular Biology Faculty of the Center for Cancer Research, NCI, Translational Faculty Development Committee, Mentor, Physician-Scientist Program, MDACC
1999-2003	Associate Attending Physician, Associate Professor of Medicine & Cancer Biology, Department of Genitourinary Medical Oncology, UT MD Anderson Cancer Center, Houston, TX
1998-1999	Staff Scientist, The Burnham Institute, La Jolla, CA

Honors

2023	Torian Barineau Fund Award
2021-present	eLife Reviewing Editor for Medicine and Cancer Biology
2021-present	The Levy-Longenbaugh Foundation Award
2017	Dr. Ronaldo Ribeiro Memorial Lecture and Prize
2010	Edith and Peter O'Donnell Award, The Academy of Medicine, Engineering and Science of Texas
2006	Named Fellow of the M.D. Anderson Research Trust
2003	The American Society for Clinical Investigation, Inducted "Young Turk"
2002	The Randall-Downey Foundation Award
2001	The V Foundation on Translational Cancer Research Award
2000-2020	The Gillson Longenbaugh Foundation Award

C. Contributions to Science

1. End-of-life patients and their families who participated in a carefully designed and implemented study protocol provided a unique opportunity to map the human vasculature. Multiple patients have been studied, leading to millions of peptides recovered from tissues and organs throughout the body. One of the original findings from this extensive body of work ultimately led to a first-in-man trial in castrate-resistant metastatic prostate cancer patients. This programmatic effort led to the identification of the interleukin-11 receptor alpha (IL-11R) as a marker of advanced and metastatic prostate cancer, and this marker was ultimately the target we investigated in our first-in-man clinical trial in patients with metastatic prostate cancer, as reported by Pasqualini et al. Thirteen US patents have been issued for technology and targeting agents derived from the phage display and vascular mapping programs.

    a. 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.
    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. Pentz RD, Flamm AL, Pasqualini R, Logothetis CJ, **Arap W**. Revisiting ethical guidelines for research with terminal wean and brain-dead participants. Hastings Cent Rep. 2003 Jan-Feb;33(1):20-6. PMID: 12613384.
    d. **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.

2. Screening combinatorial peptide libraries by *in vitro* phage display of serum antibodies from prostate cancer patients identified GRP78 as a highly expressed cell surface protein in prostate and breast tumors as well as leukemias. Using the patient-derived osteogenic prostate tumor, MDA-PCa-118b, we identified a novel GRP78 binding peptide, SNTRVAP. Recently, we identified human recombinant anti-GRP78 antibodies by screening a combined yeast/phage antibody display library. There are three pending patent applications related to anti-GRP78 antibodies for therapeutic applications.

    a. D'Angelo S, Staquicini FI, Ferrara F, Staquicini DI, Sharma G, Tarleton CA, Nguyen H, Naranjo LA, Sidman RL, **Arap W**, Bradbury AR, Pasqualini R. Selection of phage-displayed accessible recombinant

targeted antibodies (SPARTA): methodology and applications. JCI Insight. 2018 May 3;3(9):e98305. PMID: 29720567; PMCID: PMC6012512.

b. Staquicini DI, D'Angelo S, Ferrara F, Karjalainen K, Sharma G, Smith TL, Tarleton CA, Jaalouk DE, Kuniyasu A, Baze WB, Chaffee BK, Hanley PW, Barnhart KF, Koivunen E, Marchiò S, Sidman RL, Cortes JE, Kantarjian HM, **Arap W**, Pasqualini R. Therapeutic targeting of membrane-associated GRP78 in leukemia and lymphoma: preclinical efficacy in vitro and formal toxicity study of BMTP-78 in rodents and primates. Pharmacogenomics J. 2018 May 22;18(3):436-443. PMID: 29205207.

c. Mandelin J, Cardó-Vila M, Driessen WH, Mathew P, Navone NM, Lin SH, Logothetis CJ, Rietz AC, Dobroff AS, Proneth B, Sidman RL, Pasqualini R, **Arap W**. Selection and identification of ligand peptides targeting a model of castrate-resistant osteogenic prostate cancer and their receptors. Proc Natl Acad Sci USA. 2015 Mar 24;112(12):3776-81. PMID: 25762070; PMCID: PMC4378428.

d. Mintz PJ, Kim J, Do KA, Wang X, Zinner RG, Cristofanilli M, Arap MA, Hong WK, Troncoso P, Logothetis CJ, Pasqualini R, **Arap W**. Fingerprinting the circulating repertoire of antibodies from cancer patients. Nat Biotechnol. 2003 Jan;21(1):57-63. PMID: 12496764.

3. We have combined the high cell transduction capability of adeno-associated virus with cell targeting by bacteriophage into a hybrid vector termed AAVP. By bioengineering a cassette containing genes encoding the Herpes simplex virus thymidine kinase in AAVP, we demonstrated that implanted tumors could be specifically targeted by systemic administration, non-invasively imaged in the presence of [^{18}F]-FEAU and treated with ganciclovir to arrest tumor growth. Two US patents have been granted describing the AAVP technology and oncology applications.

   a. 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 tumor-associated macrophages in triple-negative breast cancer. Elife. 2021 Jun 1;10:e65145. PubMed PMID: 34060472; PMCID: PMC8169110.

   b. 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):12780-12785. PubMed PMID: 27791177; PubMed Central PMCID: PMC5111698.

   c. Ferrara F, Staquicini DI, Driessen WH, 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):12786-12791. PMID: 27791181; PMCID: PMC5111687.

   d. Staquicini FI, Ozawa MG, Moya CA, Driessen WH, Barbu EM, Nishimori H, Soghomonyan S, Flores LG 2nd, Liang X, Paolillo V, Alauddin MM, Basilion JP, Furnari FB, Bogler O, Lang FF, Aldape KD, Fuller GN, Höök M, Gelovani JG, Sidman RL, Cavenee WK, Pasqualini R, **Arap W**. Systemic combinatorial peptide selection yields a non-canonical iron-mimicry mechanism for targeting tumors in a mouse model of human glioblastoma. J Clin Invest. 2011 Jan;121(1):161-73. PMID: 21183793; PMCID: PMC3007161.

4. We have further engineered the phage genome to divergent goals: capsid modifications were introduced to allow the particles to display the penetration peptide sequence on the major pVIII coat protein, allowing receptor independent cell entry. Furthermore, 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. Additionally, phage particles displaying peptides that mediate the crossing of the air-blood barrier in the lungs enable

pulmonary delivery of phage in mice and non-human primates to elicit a systemic and specific humoral response. This was evaluated in for utility in the design and optimization of immunogenic phage particles for use in SARS-CoV-2 infection. 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. PubMed PMID: 34234013; PMCID: PMC8325333.
b. 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.
c. 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. Sci Rep. Intracellular targeting of annexin A2 inhibits tumor cell adhesion, migration, and in vivo grafting. 2017 Jun 26;7(1):4243. PMID: 28652618; PMCID: PMC5484684.
d. 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.

5. To further evaluate our various targeting capabilities, we have also been 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. Three US patents have been issued for our nanotechnology program for patterning cells with magnetic guidance.

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. 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 USA. 2016 Feb 16;113(7):1877-82. PMID: 26839407; PMCID: PMC4763738.
c. Salameh A, Lee AK, Cardó-Vila M, Nunes DN, Efstathiou E, Staquicini FI, Dobroff AS, Marchiò S, Navone NM, Hosoya H, Lauer RC, Wen S, Salmeron CC, Hoang A, Newsham I, Lima LA, Carraro DM, Oliviero S, Kolonin MG, Sidman RL, Do KA, Troncoso P, Logothetis CJ, Brentani RR, Calin GA, Cavenee WK, Dias-Neto E, Pasqualini R, **Arap W**. PRUNE2 is a human prostate cancer suppressor regulated by the intronic long noncoding RNA PCA3. Proc Natl Acad Sci USA. 2015 Jul 7;112(27):8403-8. PMID: 26080435; PMCID: PMC4500257.
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 USA. 2006 Jan 31;103(5):1215-20. PMID: 16434473; PMCID: PMC1346765.

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