UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

Update Your Profile

Vincent C.O. Njar, PhD, (UCL/London)

Academic Title:

Professor

Primary Appointment:

Pharmacology

Additional Title:

Head, Medicinal Chemistry Section, Center for Biomolecular Therapeutics (CBT); Institute for Bioscience and Biotechnology Research (IBBR)

Email:

vnjar@som.umaryland.edu

Location:

685 West Baltimore Street, HSF 1 Suite: 580-E, Baltimore, MD 21201; 9600 Gudelsky Drive, Suite 314-B, Rockville, MD 20850

Phone (Primary):

410-706-6364 (Baltimore); 240-314-6448 (Rockville)

Fax:

410-706-0332 (Baltimore); 240-314-6255 (Rockville)

Download CV

Professor

Head, Medicinal Chemistry Section, Center for Biomolecular Therapeutics (CB); Institute for Bioscience and Biotechnology Research (IBBR)

Email: vnjar@som.umaryland.edu

Location: 685 West Baltimore Street, HSF 1 Suite: 580-E, Baltimore

Phone (Primary):410-706-6364 (Baltimore); 240-314-6448 (Rockville)

Fax: 410-706-0332 (Baltimore); 240-314-6255 (Rockville)

Education and Training

- University of Ibadan, Ibadan, Nigeria, B.Sc. (Hons), Chemistry, 1976
- University of London (University College, London), United Kingdom, Ph.D. Organic Chemistry, 1980
- Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts, USA, Postdoctoral Fellowship, 1980-1982

Boisketch

Dr. Vincent Njar has a long standing interest in the rational discovery and development of small molecules as anti-cancer agents. He is a leading medicinal chemist and oncopharmacologist who has made significant discoveries in the development of novel small molecules with potential for the treatments of a variety of cancers, especially breast, prostate and pancreatic cancers. Dr. Njar invented novel reactions that led to the synthesis novel inhibitors of all-trans retinoic acid (ATRA) metabolism enzyme (CYP26). These inhibitors are also referred to as retinoic acid metabolism blocking agents (RAMBAs). Some of our compounds are by far the most potent RAMBAs known. These inhibitors may be useful in enhancing the levels of endogenous ATRA, causing 'ATRA-mimetic' effects without the need for ATRA administration. Some of our novel RAMBAs are potent inhibitors of growth of both breast and prostate cancer cells and they are also strong inhibitors of breast and prostate cancer tumors in animal xenograft models.

In ongoing studies, we have discovered that our novel RAMBA retinamides, now called novel retinamides (NRs) also antagonize transactivation of the androgen receptor (AR), degrade the full-length and splice variant ARs in human prostate cancer cell lines. In addition, the NRs exquisitely cause degradation of MAP kinase-interacting kinases (Mnk 1 and 2) with concomitant blockade of eukaryotic translation initiation factor 4E (eIF4E) cap dependent translation initiation in both human breast and prostate cancer cell lines. Altogether, these effects of NRs in breast and prostate cancer cell lines promotes apoptosis, impede cell growth, cell proliferation and matrix invasion in these cell lines, making the NRs strong candidates for development as novel anti-breast/prostate cancer therapeutics. To the best of our knowledge, our NRs are the first MAP kinase-interacting kinases (Mnk 1/2) degrading agents (MNKDAs) known. Further development of these agents are ongoing in collaboration with Terpene Pharmaceuticals LL, a small business founded by Dr. Njar in 2014.

In collaboration with Angela Brodie, Ph.D., internationally renowned breast cancer researcher, we developed some of the most potent inhibitors of CYP17 known. Some of these novel CYP17 inhibitors are also potent androgen receptor (AR) antagonists (anti-androgens), strong degraders of AR and its splice variants. Our clinical candidate galeterone (gal; formerly called VN/124-1 or TOK-001) successfully advanced through Phase I and II studies (under an exclusive license by University of Maryland, Baltimore (UMB) to Tokai Pharmaceuticals Inc.), showing that gal was well tolerated with promising clinical activity in men with castration resistant prostate cancer (CRCP). Phase III trial, ARMOR3-SV, was launched in which enzalutamide was compared to gal in patients with mCRPC expressing an AR-V7 splice variant, with the primary endpoint being radiographic progression free survival (rPFS). However, a recent interim analysis by the independent Data Monitoring Committee revealed that the primary endpoint was unlikely to be met, and therefore the trial was discontinued, though no safety concerns were cited.

In our efforts to discover and develop the next generation galeterone analogs (NGGAs), we have discovered that gal and the NGGAs degrade Mnk1/2 to disrupt the rate-limiting

eukaryotic translational initiation factor 4E (eIF4E) signaling, thus causing inhibition of tumor growth, metastasis and treatment resistance in various cancers. Gratifyingly, the lead NGGAs have superior efficacies and pharmaceutical properties compared to gal.

Research/Clinical Keywords

Medicinal Chemistry, oncopharmacology, anti-cancer drug discovery and development, small-molecule design and synthesis, cancers (breast, prostate, pancrease, skin), steroidal compounds, retinoidal compounds, steroid and retinoid-mimetics, pharmacokinetics, anti-tumor xenograft studies, inhibitors of CYP26, CYP17 and CYP19 (aromatase), AR antagonists, AR/AR-Vs degraders, Mnk1/2 degraders, inhibitors of oncogenic protein translation, Mnk1/2, eukaryotic translation initiation factor 4F/ eukaryotic initiation factor 4E, inhibitors of tumor growth and metastasis, mechanisms of action of anti-cancer agents.

Highlighted Publications

Njar VCO, Klus GT, Brodie AMH. Nucleophilic vinylic “addition-elimination” substitution reaction of 3β-acetoxy-17-chloro-16-formylandrosta-5,16-diene: A novel

and general route to 17-substituted-Δ16 steroids. Part 1. Synthesis of novel 17-azolyl-

Δ16 steroids; inhibitors of 17α-hydroxylase/17,20-lyase (17α-lyase). Bioorg. Med.

Chem. Lett., 1996, 6:2777-2782.

Njar VCO, Kato K, Nnane IP, Grigoryev DN, Long BJ, Brodie, A. M. H. Novel 17-azolyl steroids; potent inhibitors of cytochrome 17α-hydroxylase/17,20-lyase (P45017α): Potential agents for the treatment of prostate cancer. J. Med. Chem., 1998, 41:902-912.

Handratta VD, Vasaitis TS, Njar VCO, Kataria R, Chopra P, Newman Jr. D, Farquhar, R, Brodie AMH.# Novel C-17-Heteroaryl Steroidal CYP17 Inhibitors/Antiandrogens: Synthesis, Pharmacokinetics and Antitumor Activity in the LAPC4 Human Prostate Cancer Xenograft Model. J. Med. Chem., 2005, 48:2972-2984.

Purushottamachar P, Godbole AM, Gediya LK, Martin MS, Vasaitis TS, Kwegyir-Afful AK, Ates-Alagoz Z, Njar VCO. Systematic Structure Modifications of Multi-target Prostate Cancer Drug Candidate Galeterone to Produce Novel Androgen Receptor Down-regulating Agents as an Approach to Treatment of Advanced Prostate Cancer. J. Med. Chem., 2013, 56: 4880-4898.

Ramalingam S., Gediya LK, Kwegyir-Afful AK, Purushottamachar P., Vidya P. Ramamurthy VP, Mbatia M, and Njar VCO. First MAP Kinase Interacting Kinase 1 Degrading Agents Block Phosphorylation eIF4E, Induce Apoptosis, Inhibit Cell Growth, Migration and

Invasion in Triple Negative and HER2-overexpressing Breast Cancer Cell Lines. Oncotarget, 2014, 5: 530-543.

Kwegyir-Afful AK, Purushottamachar P., Ramalingam S., Vidya P. McCarty D, Ramamurthy VP, and Njar VCO. Galeterone and VNPT-55 induce proteasomal degradation of AR/AR-V7, induce significant apoptosis and suppress growth of castration prostate cancer xenografts. Oncotarget. 2015, 6:27440-27460. PMID: 26196320.

Kwegyir-Afful AK, Bruno RD, Purushottamachar P, Murigi FN, Njar VC. Galeterone and VNPT55 disrupt Mnk-eIF4E to inhibit prostate cancer cell migration and invasion. FEBS J. 2016, 283(21):3898-3918. PMID: 27618366.

Kwegyir-Afful AK, Murigi FN, Purushottamachar P, Ramamurthy VP, Martin MS, Njar VC. Galeterone and its analogs inhibit Mnk-eIF4E axis, synergize with gemcitabine, impede pancreatic cancer cell migration, invasion and proliferation and inhibit tumor growth in mice. Oncotarget. 2016 Dec 24. doi: 10.18632/oncotarget.14154. [Epub ahead of print]; PMID: 28030797.

Ramamurthy VP, Ramalingam S, Kwegyir-Afful AK, Hussain A, Njar VC. Targeting of protein translation as a new treatment paradigm for prostate cancer. Curr Opin Oncol., 2017, 29: 210-220. PMID: 28282343.

Awards and Honors

- Lecturer II, Department of Chemistry, University of Ibadan, Ibadan, Nigeria, 1982-1985
- Lecturer I, Department of Chemistry, University of Ibadan, Ibadan, Nigeria, 1985-1988
- Senior Lecturer, Department of Chemistry, University of Ibadan, Ibadan, Nigeria, 1988-1993
- Reader, Department of Chemistry, University of Ibadan, Ibadan, Nigeria, 1993-1996
- Professor, Department of Chemistry, University of Ibadan, Ibadan, Nigeria, 1996-1999
- Visiting Professor*, Department of Pharmacology & Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD, USA. *(Periodically returning to my home institution, University of Ibadan, Ibadan, Nigeria), 1996-1999
- Full Member, Marlene and Stewart Greenabaum Cancer Center, UMB, Baltimore, MD, USA, 1999-2008
- Associate Professor, Department of Pharmacology & Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD, USA. 2002-2008.
- Professor, Department of Pharmaceutical Sciences, Jefferson School of Pharmacy, Thomas Jefferson University, Philadelphia, PA, USA, 2008-2011

- Full Member, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, USA, 2008-2011

- Consultant for Tokai Pharmaceutics, Boston, MA, USA, 2008-2016

- Member, Clinical Cancer Research Review Committee (CCRRC), Kimmel Cancer Center, 2009-2011

- Member, Jefferson Scholl of Pharmacy Executive Council, 2009-2011

- Member, Thomas Jefferson University Faculty Senate, 2010-2011

- Professor, Department of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD, USA, 2012 - Present

- Medicinal Chemistry Group Leader, The University System of Maryland Center for Biomolecular Therapeutics (CBT), 2012 - Present

- Full Member, Marlene and Stewart Greenabaum Cancer Center, UMB, Baltimore, MD, USA, 2012 - Present

- Member, Appointment, Promotion and Tenure Committee, University of Maryland School of Medicine, Baltimore, MD, USA, 2013 - 2016

- Founder, Member of the Board of Directors, Chief Scientific Officer, Terpene Pharmaceuticals LLC, 2014 - Present

 Update Your Profile