OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

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NAME: Newman, Amy Hauck

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

POSITION TITLE: Acting Scientific Director and Chief, Molecular Targets and Medications Discovery Branch and Medicinal Chemistry Section

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 |
| --- | --- | --- | --- |
| Mary Washington College | B.S. | 05/1980 | Chemistry |
| Medical College of Virginia, Virginia Commonwealth University | Ph.D. | 05/1985 | Medicinal Chemistry |
| NIDDK, National Institutes of Health | Postdoctoral | 12/1987 | Medicinal/Organic Chemistry |

1. **Personal Statement**

My research effort is focused on the design and synthesis of novel ligands to study the structure and function of selected G-protein coupled receptors and monoamine transporters associated with substance use disorders. Highly selective compounds are prepared for characterization of these molecular targets and to develop structure-activity relationships within diverse chemical classes of drugs. In addition, specific tools such as fluorescent and radiolabeled ligands are synthesized for receptor or transporter structure-function studies. My research program is currently studying the monoamine transport systems and the dopamine D2 receptor family (D2/D3) through the design, synthesis and pharmacological evaluation of novel ligands. The combination of state of the art synthetic organic chemistry, computational biophysics and interpretation of pharmacological data has resulted in the discovery of important molecular probes for studying these neurochemical targets. It is envisioned that ultimately this multidisciplinary approach will provide new leads toward the development of potential pharmacotherapeutic agents for the treatment of substance use disorders. Over the years the strong collaborations I have established with many respected researchers in the field have led to the significant advancement of potential therapeutic agents in preclinical studies of drug abuse and medication development. These collaborative efforts have yielded >280 publications in peer-reviewed journals and 13 U.S. patents or patent applications, several of which have been licensed by pharmaceutical companies.

**B. Positions and Honors**

**Positions and Employment**

1985 - 1988 NRSA Post-doctoral fellow, Section on Drug Design and Synthesis, NIDDK, Bethesda,

Maryland

1988 - 1990 Research Chemist, Department of Applied Biochemistry, Walter Reed Army Institute of

Research, Washington D.C.

1991 - 1994 Senior Staff Fellow, Psychobiology Section, NIDA-IRP, Baltimore, Maryland

1994 - 1999 Investigator (tenure track), Psychobiology Section, NIDA-IRP, Baltimore, Maryland

1999 - Senior Investigator (tenured) and Chief, Medicinal Chemistry Section, NIDA-IRP, Baltimore,

Maryland

2011 - Deputy Scientific Director; Chief, Molecular Targets and Medications Discovery

Branch and Director, NIDA-IRP Medication Development Program, Baltimore, Maryland

2018 - Acting Scientific Director, NIDA-IRP

2020- Scientific Director, NIDA-IRP

**Honors**

1998 Sato International Memorial Award - Awarded by the Pharmaceutical Society of Japan in

March 1999, Tokushima, Japan

2004 NIDA Director’s Award of Merit

2006 NIDA Director’s Award for EEO, Diversity and Quality of Worklife

2009 1st recipient of the NIDA/NIH Women Scientists Advisory Achievement Award

2010NIDA Director’s Award of Merit

2010 Elected member of the American College of Neuropsychopharmacology

2012 1st recipient of the NIDA Scientific Director’s Innovators Partnership Program Award

2013 NIDA-IRP Diversity Mentoring Award for Faculty

2014 Marian W. Fischman Lectureship Award, College on Problems of Drug Dependence

2015 NIDA Director’s Innovation Award

2016 Philip Portoghese Lectureship Award, Division of Medicinal Chemistry and the Journal of Medicinal Chemistry, American Chemical Society (first woman recipient)

2018 NIH OD Honor Award - as a member of the NIH Tenure-Track Mentoring Program and a co-leader of the NIDA-NIA TTI Mentoring Program

2018 Honored as a “Remarkable Woman in Medicinal Chemistry” at the 255th American Chemical Society National Meeting

2018 NIH Office of the Director Honor Award - as a member of the NIH Tenure-Track Mentoring Program and a co-leader of the NIDA-NIA TTI Mentoring Program

2019 NIH Ruth L. Kirschstein Mentoring Award, NIH Office of the Director

C. Contributions to Science

1. Design, synthesis, structure-activity relationships (SAR) and in vivo development of novel dopamine D3 receptor antagonists and partial agonists for the treatment of substance use disorders. Developing novel ligands and SAR for the D2-like family receptors, and especially for the D3 receptor has not only provided important preclinical tools for potential translation, but critical information to put into context the structure and function of this receptor subtype. PG01037, from the Newman lab, is now commercially available. Two patents have recently been licensed for development of lead molecules toward opioid use disorders.

1. Kumar, V., Bonifazi, A., Ellenberger, M. P., Keck, T. M., Pommier, E., Rais, R., Slusher, B. S., Gardner, E.; You, Z.-B.; Xi, Z-X.; Newman A. H. (2016) Highly selective D3R antagonists and partial agonists based on eticlopride and the D3R crystal structure: new leads for opioid dependence treatment. Journal of Medicinal Chemistry*,* 59(16)*,* 7634-7650. PMID: 27508895
2. You, Z.-B., Bi, G., Galaj, E., Kumar, V., Cao, J., Gadiano, A., Rais, R., Slusher, B.S., Gardner, E.L., Xi, Z.X., & Newman, A.H. (2019). Dopamine D3R antagonist VK4-116 attenuates oxycodone self-administration and reinstatement without compromising its antinociceptive effects. Neuropsychopharmacology, 44(8), 1415-1424. PMID: 30555159
3. Shaik, A. B., Kumar, V., Bonifazi, A., Guerrero, A. M., Cemaj, S. L., Gadiano, A., Lam, J., Xi, Z.-X., Rais, R., Slusher, B. S., Newman A. H. (2019) Investigation of novel primary and secondary pharmacophores, and 3-substitution in the linking chain of a series of highly selective and bitopic dopamine D3 receptor antagonists and partial agonists. *Journal of Medicinal Chemistry*, *62(20),* 9061-9077. PMID:31526003

2. The development of biased or allosteric GPCR ligands has become an exciting strategy toward discovering novel molecules that may have therapeutic applications in treating neuropsychiatric disorders. We have recently discovered a series of D2-like agonists that are G-protein (over beta-arrestin) biased and a second series of bitopic molecules that exhibit allosteric pharmacology at D3R.

1. Bonifazi, A., Yano, H., Ellenberger, M. P., Muller, L., Kumar, V., Zou, M., Cai, N.S., Guerrero, A.M., Woods, A.S., Shi, L., & Newman, A.H. (2017). Novel bivalent ligands based on the sumanirole pharmacophore reveal dopamine D2 receptor (D2R) biased agonism. Journal of Medicinal Chemistry,60(7), 2890-2907. PMID: 28300398
2. Bonifazi, A., Yano, H., Guerrero, A.M., Kumar, V., Hoffman A.F., Lupica, C.R., & Newman, A.H. (2019). Novel and Potent Dopamine D2 Receptor Go-Protein Biased Agonists, ACS Pharmacology and Translational Science, 2(1), 52-65. PMCID: PMC6371206
3. Newman, A. H., Battiti, F. O., Bonifazi, A. (2020) 2016 Philip S. Portoghese Medicinal Chemistry Lectureship: Designing Bivalent or Bitopic Molecules for G-protein Coupled Receptors - The Whole is Greater Than the Sum of its Parts. Journal of Medicinal Chemistry*, 62(20)* 9061-9078. PMID: 31499001

3. Translating the atypical dopamine uptake inhibitor hypothesis with R-modafinil and novel analogues. We identified R-modafinil as a unique dopamine uptake inhibitor that has the potential of translation to the clinic as a medication to treat psychostimulant abuse and the cognitive impairment that develops with chronic drug abuse. We have synthesized hundreds of novel analogues of modafinil and identified several lead agents that are superior to the parent molecule, in animal models of psychostimulant abuse.

1. Loland, C. J., Mereu, M., Okunola, O. M., Cao, J., Prisinzano, T. E., Mazier, S., Kopajtic, T., Shi, L., Katz, J.L., Tanda, G., & Newman, A.H. (2012). R-modafinil (armodafinil): A unique dopamine uptake inhibitor and potential medication for psychostimulant abuse. Biological Psychiatry, 72(5), 405-413. PMID: 22537794
2. Cao,J., Slack, R. D., Bakare, O. M., Burzynski, C., Rais, R., Slusher,B. S., Kopajtic, T., Bonifazi, A., Ellenberger, M. P., Yano, H., He, Y., Bi, G.-H., Xi, Z.-X., Loland,C. J., Okunola-Bakare, Y., Newman, A. H. Novel and High Affinity 2-[(Diphenylmethyl)sulfinyl]acetamide (Modafinil) Analogues as Atypical Dopamine Transporter Inhibitors. Journal of Medicinal Chemistry*,* 59(23)*,* 10676-10691*.* PMID: 27933960
3. Newman A. H., Cao, J., Keighron, J.D., Jordan, C.J., Bi, G., Liang, Y., Abramyan, A.M., Avelar, A.J., Tschumi, C.W., Beckstead, M.J., Shi, L., Tanda, G., & Xi, X-Z. (2019). Translating the atypical dopamine uptake inhibitor hypothesis toward therapeutics for treatment of psychostimulant use disorders. Neuropsychopharmacology,44(8)*,* 1435-1444. PMID: 30858517

4. Discovery of the benztropine class of atypical dopamine uptake inhibitors as pharmacotherapies for psychostimulant abuse. In addition to pioneering this area of research, we developed several lead compounds as potential pharmacotherapies. Two patents have been licensed by Pharma and several benztropine analogues are commercially available for preclinical investigation.

1. Newman, A. H., Kline, R.H., Allen, A.C., Izenwasser, S., George, C., & Katz, J.L. (1995). Novel 4'-substituted and 4',4''-disubstituted 3-alpha-(diphenylmethoxy)tropane analogs as potent and selective dopamine uptake inhibitors. Journal of Medicinal Chemistry, 38(20), 3933-40. PMID: 7562926
2. Hiranita, T., Soto, P.L., Newman, A.H., & Katz, J.L. (2009). Assessment of reinforcing effects of benztropine analogs and their effects on cocaine self-administration in rats: Comparisons with monoamine uptake inhibitors. Journal of Pharmacology and Experimental Therapeutics, 329(2), 677-686. PMID: 19228996
3. Hiranita, T., Wilkinson, D., Hong, W., Zou, M., Kopjtic, T., Soto, P., Lupica, C.R., Newman, A.H., & Katz, J.L. (2014). 2-isoxazol-3-phenyltropane derivatives of cocaine: Molecular and atypical system effects at the dopamine transporter. Journal of Pharmacology and Experimental Therapeutics, 349(2), 297-309. PMID: 24518035
4. Zou, M.F., Cao, J.J., Abramyan, A.M., Kopajtic, T., Zanettini, C., Guthrie, D.A., Rais, R. , Slusher, B.S., Shi, L., Loland, C.J., & Newman, A.H. (2017). Structure-activity relationship studies on a series of 3 alpha-[bis(4-fluorophenyl)methoxy]tropanes and 3 alpha-[bis(4-fluorophenyl)methylamino]tropanes as novel atypical dopamine transporter (DAT) inhibitors for the treatment of cocaine use disorders. Journal of Medicinal Chemistry, 60(24), 10172−10187.PMD: 29227643

5. Development of novel DAT, SERT or D2- Dopamine receptor selective photoaffinity and/or fluorescent ligands for structure function studies. These tools have proven highly useful in numerous laboratories for structure-function and visualization studies. They have also provided the basis for developing similar tools in numerous other labs. Several of our fluorescent ligands, such as JHC1-064, are currently being used for single molecule fluorescence studies.

1. Hansen, F. H., Skjorringe, T., Yasmeen, S., Arends, N., Sahai, M., Erreger, K., Andreassen, T.F., Holy, M., Hamilton, P.J., Neergheen, V., Karlsbor, M., Newman, A.H., Pope, S., Heales, S.J.R, Friberg, L., Law, I., Pinborg, L.H., Sitte, H.H., Loland, C., Shi, L., Weinstein, H., Galli, A., Hjermind, L.E., Moller, L.B., & Gether, U. (2014). Missense dopamine transporter mutations associate with adult parkinsonism and ADHD. Journal of Clinical Investigation,124(5), 3107-3120. PMID: 24911152
2. Silm, K., Yang, J., Marcott, P. F., Asensio, C. S., Eriksen, J., Guthrie, D. A., Newman, A.H., Ford, C.P., & Edwards, R.H. (2019). Synaptic vesicle recycling pathway determines neurotransmitter content and release properties. Neuron,102(4)*,* 786-800*.* PMID: 31003725
3. Guthrie, D. A., Herenbrink, C. K., Lycas, M. D., Ku, T., Bonifazi, A., DeVree, B. T., Mathiasen, S. Javitch, J. A., Grimm, J. B., Lavis, L., Gether, U., Newman A. H. (2020) Novel Fluorescent Ligands Enable Single-Molecule Localization Microscopy of the Dopamine Transporter. ACS Chemical Neuroscience, 11(20)3288-3300. PMID: 32926777

**Complete List of Published Work in MyBibliography:** https://www.ncbi.nlm.nih.gov/pubmed/?term=Newman+AH

D. Additional Information: Research Support

As a senior investigator at the NIDA-Intramural Research Program since 1991, my research budget is funded entirely and directly through the NIDA-IRP.

**Ongoing Research Support**

ZIA DA000389 Newman (PI) 10/01/1991 – Ongoing

NIDA Novel and Atypical Dopamine Uptake Inhibitors

ZIA DA000424 Newman (PI) 10/01/1999 – Ongoing

NIDA Novel Dopamine D3 Receptor Ligands

Z1A DA000609 Newman (PI) 10/01/2016 – Ongoing

NIDA Dopamine D2-like Functionally Selective Agonists

Z1A DA000610 Newman (PI) 10/01/2016 – Ongoing

NIDA Monoamine Transporter Nanoprobes