BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Khan, Arshad Mahmood	Assistant Professor
eRA COMMONS USER NAME (credential, e.g., agency login) arshadk	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of California, Riverside, CA	B.S.	06/94	Biology/Biochemistry (double major)
University of California, Riverside, CA	M.S.	12/96	Biochemistry
University of California, Riverside, CA	Ph.D.	03/02	Neuroscience
Univ. of Southern California, Los Angeles, CA	Postdoc.	06/07	Neuroendocrinology and Neuroanatomy

A. Personal Statement

The research goal of my laboratory is to identify the neural substrates underlying complex, motivated behaviors and physiological processes such as feeding, drinking, and autonomic/metabolic function. **Our long-term aim is to identify novel molecular targets for drug treatments against metabolic disorders such as diabetes and obesity**. For example, I use rodent models to identify nutrient sensing and feeding control circuits in a brain region known as the hypothalamus, and determine how these circuits make connections with other brain regions that control the rewarding and reinforcing aspects of food. In order to achieve these goals, our laboratory is identifying, at high resolution, various neuronal populations expressing behavioral control neuropeptides; these are located in several hypothalamic nuclei. All of these neuropeptides are being visualized using multi-fluorescent immunocytochemistry. In this proposal to use the QExactive instrument within the BBRC BACF core, we hope to extend our analyses of these neuropeptides using mass spectrometry. **I am working closely with the PI of the current proposal, Dr. Igor Almeida, and Dr. Nathan VerBerkmoes (the BACF core manager) to use laser-capture microdissection methods to harvest tissue samples from the brains of hypoglycemic or overnight-fasted male and female rats, and to analyze the proteomic and peptidomic repertoires of these samples relative to control (normoglycemic or fed) animals**. I have over a decade's experience in hypothalamic neurochemistry and identifying biomarkers in hypothalamic tissue.

Publications relevant to the proposed research:

1. **Khan AM**, Stanley BG, Bozzetti L, Chin C, Stivers C, Currás-Collazo MC. (2000) *N*-methyl-D-aspartate receptor subunit NR2B is widely expressed throughout the rat diencephalon: An immunohistochemical study. *The Journal of Comparative Neurology*, 428:428-449.
2. Burns GAPC, **Khan AM**, Cheng W, Watts AG. (2005) A 'Stress-Management' System: Computational knowledge representation of experiments that delineate neural circuits and histochemical expression patterns based on the primary literature and raw data. *American Neuroendocrine Society, 2005 Workshop on the Neuroendocrinology of Stress.*
3. **Khan AM**, Kaminski KL, Sanchez-Watts G, Ponzio TA, Kuzmiski JB, Bains JS, Watts AG. (2011) MAP kinases couple hindbrain-derived catecholamine signals to hypothalamic adrenocortical control mechanisms during glycemia-related challenges. *The Journal of Neuroscience*, 31(50):18479-18491.
4. Watts AG, **Khan AM** (2013). Identifying links in the chain: The dynamic coupling of catecholamines, peptide synthesis, and peptide release in hypothalamic neuroendocrine neurons. *Advances in Pharmacology, 68:*421-444.

B. Positions and Honors

Positions and Employment

2007-2010 Research Assistant Professor, Dept. of Biological Sciences, Univ. of Southern California

Jan 2011- Adjunct Assistant Professor, Dept. of Biological Sciences, Univ. of Southern California
Jan 2011- Assistant Professor (Tenure Track), Dept. of Biological Sciences, Univ. of Texas at El Paso

Other Experience and Professional Memberships

1996- Member, Society for Neuroscience
2010- Member, American Society for Neurochemistry
2011- Member, Membership Committee, American Society for Neurochemistry
2013-2014 Co-Leader, Obesity & Metabolic Disorders Cluster, RCMI Translational Research Network
2013- Member, Sigma Xi
2010-2014 Member, Membership Committee, American Society for Neurochemistry
2013- Co-Leader: Obesity & Metabolic Disorders Research Cluster
RCMI Translational Research Network
2014- Co-Chair, Working Group on Brain Mapping & Molecular Imaging, University of Texas System Neuroscience & Neurotechnology Institute

Honors

2004 NIH NRSA Award, 4.3 percentile rank
2004 Co-recipient, eSciences Funding Award, Microsoft Research; 1 of 5 awarded out of 400
2008 NIH Mentored Career Development Grant (K01)
2010 Travel Award, Winter Conference on Brain Research
2014 Outstanding Performance Award, Office of Research and Sponsored Programs, UTEP
2015 Outstanding Performance Award, Office of Research and Sponsored Programs, UTEP

C. Contributions to Science

1. Molecular Basis of Feeding Behavior: This body of work provided some of the first evidence for key signal transduction cascades to be involved in modulating feeding behavior within the hypothalamus. In particular, they are the first to examine protein tyrosine kinase involvement in feeding stimulation, and also confirm and extend findings involving the cyclic AMP signaling cascade. This work is significant because it remains unique in the field in providing key linkages between ionotropic glutamate receptors, second messenger systems and feeding control mechanisms in the rodent hypothalamus. Prior to these studies, no work had been done to directly implicate tyrosine kinase signaling cascades in glutamate receptor-delimited feeding control; this work confirmed and extended the functional connections for these molecules established in other regions of the brain (e.g., hippocampus, cortex) and extended them by providing direct evidence for their role in the control of motivated behaviors.

    a. Gillard ER, **Khan AM**, Mouradi B, Nalamwar O, Stanley BG. (1998) Eating induced by perifornical cAMP is behaviorally selective and involves protein kinase activity. *American Journal of Physiology*, *275*:R647-R653. PMID: 9688705.
    b. Gillard ER, **Khan AM**, Grewal RS, Mouradi B, Wolfsohn SD, Stanley BG. (1998) The second messenger cyclic AMP elicits eating by an anatomically specific action in the perifornical hypothalamus. *The Journal of Neuroscience*, *18*:2646-2652. PMID: 9502822.
    c. **Khan AM**, Currás MC, Jamal FA, Turkowski CA, Goel RK, Dao J, Gillard ER, Wolfsohn SD, Stanley BG. (1999) Lateral hypothalamic NMDA receptor subunits NR2A and/or NR2B mediate eating: Immunochemical/behavioral evidence. *American Journal of Physiology*, *276*:R880-R891. PMID: 10070151.
    d. **Khan AM**, Cheung HH, Gillard ER, Palarca JA, Welsbie DS, Gurd JW, Stanley BG. (2004) Lateral hypothalamic signaling mechanisms underlying feeding stimulation: Differential contributions of Src family tyrosine kinases to feeding triggered either by NMDA injection or by food deprivation. *The Journal of Neuroscience*, *24*:10603-10615. PMID: 15564576.

2. Circuit Basis of Neuroendocrine Responses to Glycemic Challenge: The major contributions of these studies were to provide some of the first structural evidence for the participation of key pathways between the hindbrain and hypothalamus in producing hormonal responses to changes in blood sugar levels in the periphery. We established that blood sugar changes could be detected at the level of the hypothalamus, but only if specific hindbrain circuits connected to it were kept intact; their selective destruction prevented hypothalamic cellular responses to the plasma glucose changes. We also

identified the transmitter candidates responsible for these changes to be catecholamines (either epinephrine or norepinephrine). Together, these studies provided the first demonstrable functional linkages among a peripheral glycemic challenge, the hindbrain nutrient sensing neurons detecting the challenge, the hypothalamic neurons these neurons were connected to, the transmitter they received as a signal, and the signaling pathways mobilized to trigger hormone responses to the challenge.

a. **Khan AM**, Watts AG. (2004) Intravenous 2-deoxy-D-glucose injection rapidly elevates levels of the phosphorylated forms of p44/42 mitogen activated protein kinases (ERK1/2) in rat hypothalamic parvicellular paraventricular neurons. *Endocrinology*, *145*(1):351-359. PMID: 14525908.
b. **Khan AM**, Ponzio TA, Sanchez-Watts G, Stanley BG, Hatton GI, Watts AG. (2007) Catecholaminergic control of MAP kinase signaling in paraventricular neuroendocrine neurons *in vivo* and *in vitro*: A proposed role during glycemic challenges. *The Journal of Neuroscience*, *27*(27):7344-7360. [Article featured in the journal's "This Week in the Journal" section]. PMID: 17611287.
c. **Khan AM**, Kaminski KL, Sanchez-Watts G, Ponzio TA, Kuzmiski JB, Bains JS, Watts AG. (2011). MAP kinases couple hindbrain-derived catecholamine signals to hypothalamic adrenocortical control mechanisms during glycemia-related challenges. *The Journal of Neuroscience*, 31(50):18479-18491. PMCID: PMC3293627.
d. **Khan AM**, Walker EM, Dominguez N, Sanchez-Watts G, Watts AG. (2014). Neural input is critical for arcuate hypothalamic neurons to mount intracellular signaling responses to systemic insulin and deoxyglucose challenges in male rats: implications for communication within feeding and metabolic control networks. *Endocrinology*, 155(2):405-16. PMCID: PMC3891932.

3. <u>High Resolution Molecular and Circuit Analyses in the Brain Related to Feeding Control:</u> A major thrust of my current research work is to create a high resolution map of the rodent hypothalamus in order to develop a comprehensive strategic plan to interrogate brain circuits controlling feeding behavior. In the past and also currently, scientists have taken a "black box" approach to probing the brain to examine behavior, inserting drugs or viruses by injections into the living animal in a "blind" fashion, with little knowledge of the neural substrates they are probing other than basic stereotaxic coordinates. This is especially true of the mouse, where the circuits and axonal pathways have been poorly mapped. We have decided in my lab to use the rat model as well as the mouse model to create structural maps of the hypothalamus, and then plan on using these maps to more comprehensively target finer substrates in the region to control and examine behavior. We have begun studies in this regard that are modeled after a strategic plan I have outlined in a comprehensive review of the field in 2013 (*see below*).

    a. Watts AG, **Khan AM**, Sanchez-Watts G, Salter D, Neuner CM. (2006) Activation in neural networks controlling ingestive behaviors: What does it mean and how do we map and measure it? *Physiology and Behavior*, *89*(4):501-510. PMID: 16828817.
    b. **Khan AM** (2013). Controlling feeding behavior by chemical or gene-directed targeting in the brain: What's so spatial about our methods? *Frontiers in Neuroscience*, 7 (Article 182):1-49.
    c. De Haro B, **Khan AM.** (2014). Afferent and efferent projections of the periventricular hypothalamus: A combined anterograde and retrograde tract tracing study in the adult male rat. Program No. 256.14. *2014 Neuroscience Meeting Planner*. Washington, D.C.: Society for Neuroscience, 2014. Online.
    d. Martinez A, Pinales BE, **Khan AM.** (2014). Efferent projections of the arcuate nucleus of the hypothalamus in the adult male rat: A dual retrograde tract tracing study. Program No. 256.20. *2014 Neuroscience Meeting Planner*. Washington, D.C.: Society for Neuroscience, 2014. Online.

4. <u>Neuroinformatics-Related Explorations of Neuroscientific Data:</u> Since the beginning of my postdoctoral work at the University of Southern California, I was introduced to the emerging field of neuroinformatics, and have had the pleasure of working closely with some of the top minds in the field, since USC was one of the main centers for the Human Brain Project funded by the NIH. Although I am primarily a "wet-lab" neuroscientist by training, I worked closely with personnel in the laboratories of Dr. Larry W. Swanson in Biology and Dr. Shahram Ghandeharizadeh in Computer Science. With these investigators, I collaborated on a number of neuroinformatics-related projects, and co-authored a study with them which was published in the inaugural issue of *Neuroinformatics* (see below). The main contributions to this emerging field from my own research include the proof-of-concept development of

one of the first electronic laboratory management systems for neuroscientific data in neuroendocrinology. We also pioneered the construction of "knowledge models" for this sub-discipline of neuroscience. Finally, in my current position as Director of the UTEP Systems Neuroscience Laboratory, we are developing novel data migration methods to transform spatial data mapped to one standardized brain atlas to become compatible with the spatial reference coordinate space of another rat brain atlas, thereby linking legacy data mapped in one atlas to recent data mapped in the other.

a. Burns GAPC, **Khan AM**, Ghandeharizadeh S, O'Neill MA, Chen Y-S. (2003) Practical tools and approaches for the construction of knowledge models from the neuroscientific literature. *Neuroinformatics*, 1:81-109.
b. Saxena M, Kim S-a, Burns GAPC, **Khan AM**, Su J, Hamadi Y, Ghandeharizadeh S. (2005) An overview of Sangam: A system for integrating data to investigate stress-circuitry-gene coupling. *Proceedings: First International Conference of Innovative Views of .NET Technologies (IVNET '05)*; Jun 21-22, 2005, Porto, Portugal, pp. 95-106. [Published online at: http://w2ks.dei.isep.ipp.pt/labdotnet/files/IVNET/sangam_p.pdf].
c. **Khan AM**, Hahn J, Cheng W-C, Watts AG, Burns GAPC. (2006) NeuroScholar's electronic laboratory notebook and its application to neuroendocrinology. *Neuroinformatics*, *4*(2):139-160. PMID: 16845166.
d. Wells CE, **Khan AM**. (2013). Data transformations between rat brain atlases: Mapping central microinjection sites on stereotaxically aligned and anisotropically scaled digital atlas plates in Paxinos & Watson and Swanson reference spaces. Program No. 198.06. *2013 Neuroscience Meeting Planner.* San Diego, CA: Society for Neuroscience, 2013. Online.

D. Research Support

Current Support

1. SC3 GM109817 (NIGMS) (**Khan, PI**) (04/01/2014-03/31/2018)

Identifying and mapping functional connections of feeding control neurons in the brain

This project is focused neuroanatomical tract tracing of arcuate hypothalamic circuits and mapping their topography as well as the distribution of activated arcuate neurons following peripheral leptin, ghrelin, peptide YY or insulin administration.

2. 2014 Undergraduate Science Education Grants (HHMI) (Aley, PI) (9/1/2014 – 8/31/2019)

UTEP PERSIST: UTEP Program to Educate and Retain Students In STEM Tracks

The ultimate goal of UTEP PERSIST is to significantly increase the number of exceptionally trained science and engineering graduates from the underrepresented and financially disadvantaged groups that make up the majority of UTEP's student body.

Role: Co-PI

Completed Support

1. K01 DK01897 (NIDDK) (**Khan, PI**) (09/10/2008-04/15/2013)
From glucosensing neurons to CRH neuroendocrine neurons: Circuits and signals

This project focused on defining circuits between the hindbrain and the paraventricular hypothalamus, a brain structure that helps the organism initiate responses to stressful stimuli.

2. 8G12MD007592-19 (**Khan, PI**; Llano, Co-PI) (07/01/2012-05/07/2013)

Pilot Grant: Optogenetic study of hypocretin neurons in glucosensing and hypoglycemia unawareness

The goal of this project is to rescue the autonomic responses in a rat model of hypoglycemia-associated autonomic failure by optical stimulation of neurons in the lateral hypothalamus.