Postdoc Research Fellow
Pharmacology, Physiology, and Cancer Biology
Lab of Dr. Marja Nevalainen
Job Opening ID 9292125

An excellent training opportunity for junior or senior post-doctoral fellows is available in a dynamic cancer research laboratory of Marja Nevalainen, MD, PhD, Professor, Dept. of Pharmacology, Physiology and Cancer Biology at the NCI-designated Sidney Kimmel Cancer Center at Thomas Jefferson University in Philadelphia.

The candidate will investigate Jak-Stat signaling in prostate cancer diagnostics, progression and therapy, and how Jak-Stat signaling promotes cancer progression to therapy resistant metastatic disease using human specimens as well as PDX and cell culture models. Dr. Nevalainen's group provided the proof-of-concept that Stat5 is a therapeutic target protein for prostate cancer. Her lab demonstrated that Stat5 controls prostate cancer cell viability and castrate-resistant prostate tumor growth, and Jak2-Stat5a/b signaling induces epithelial-mesenchymal transition and stem cell-like properties in prostate cancer cells. Dr. Nevalainen's lab further discovered that the Stat5 locus is amplified in castrate-resistant and metastatic prostate cancer, followed by an important translational finding that elevated active Stat5 in prostate cancer prior to intent-to-cure radical prostatectomy predicts development of castrate-resistant and metastatic spread of the disease in patients. The Nevalainen laboratory identified a family of novel small molecule Stat5 inhibitors with high efficacy in both prostate cancer and Bcr-Abl-driven leukemias. One area of current focus is on Jak2-Stat5 regulation of DNA repair in prostate cancer, the associated transcriptional programs and utilization of Jak2-Stat5 suppression as an adjuvant to radiation therapy of prostate cancer. Other major areas include investigation of the molecular mechanisms underlying Jak2-Stat5induction of lineage plasticity and regulation of androgen receptor (AR) gene transcription and the AR transcriptome in prostate cancer and translation of the concept to the clinical space.

The ideal post-doc candidate should be highly motivated and demonstrate a passion for science, innovative thinking and the ability to work independently and effectively with the other members in the team. Previous knowledge in cancer biology is required with a minimum of one peer-reviewed publication. In addition, knowledge of scientific methodologies, procedures, and basic experimental theories/applications and strong critical/analytic thinking and ability to communicate effectively are required. This postdoctoral training position includes a strong support from the mentor for career development toward an independent investigator status.

Desired Knowledge, Skills, and Abilities:

Applicants must have communications skills, knowledge of scientific approach and methodologies, and ability to design and coordinate scientific research projects. The candidate is required to perform cell culture experiments using various methodologies. The fellow may also be requested to handle laboratory animals to understand basic biochemistry. Techniques include tissue culture, transfection, western blot analysis, RNA isolation along with other state of the art

molecular, biochemical, immunohistochemistry, genomics and imaging methods. Trainees will receive training in a broad range of research methodologies and in writing scientific publications and grants. Studies involve in vivo and in vitro models of prostate cancer. Successful candidates must be organized and be able to work independently. This postdoctoral training position includes a strong support from the mentor for career development toward an independent investigator status.

Contact:

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Application Process:

Applications must contain the following documents in English.

- Curriculum Vitae, including previous positions, current position, academic title, academic distinctions, committee work, and publication list.
- A cover letter illustrating why you are the right candidate for the role.
- Names of two references.

Selected recent papers relevant to the open position:

1. Gu L, Liao Z, Hoang DT, Dagvadorj A, Gupta S, Blackmon S, Ellsworth E, Talati P, Leiby B, Zinda M, Lallas CD, Trabulsi EJ, McCue P, Gomella L, Huszar D, **Nevalainen MT.** Pharmacologic inhibition of Jak2-Stat5 signaling By Jak2 inhibitor AZD1480 potently suppresses growth of both primary and castrate-resistant prostate cancer. Clin Cancer Res. 2013 Oct 15;19(20):5658-74.

2. Liao Z, Gu L, Vergalli J, Mariani SA, De Dominici M, Lokareddy RK, Dagvadorj A, Purushottamachar P, McCue PA, Trabulsi E, Lallas CD, Gupta S, Ellsworth E, Blackmon S, Ertel A, Fortina P, Leiby B, Xia G, Rui H, Hoang DT, Gomella LG, Cingolani G, Njar V, Pattabiraman N, Calabretta B, **Nevalainen MT.** Structure-Based Screen Identifies a Potent Small Molecule Inhibitor of Stat5a/b with Therapeutic Potential for Prostate Cancer and Chronic Myeloid Leukemia. Mol Cancer Ther. 2015 Aug;14(8):1777-93 PMCID: PMC4547362. **Highlighted article and cover of the August 2015 issue.**

3. Talati PG, Gu L, Ellsworth EM, Girondo MA, Trerotola M, Hoang DT, Leiby B, Dagvadorj A, McCue PA, Lallas CD, Trabulsi EJ, Gomella L, Aplin AE, Languino L, Fatatis A, Rui H, **Nevalainen MT.** Jak2-Stat5a/b Signaling Induces Epithelial-to-Mesenchymal Transition and Stem-Like Cell Properties in Prostate Cancer. Am J Pathol. 2015 Sep;185(9):2505-22 PMCID: PMC4597281. **Subject of an Editorial.**

4. Hoang DT Iczkowski KA, Kilari D, See W, **Nevalainen MT**; "Androgen Receptor-Dependent and -Independent Mechanisms Driving Prostate Cancer Progression: Opportunities for Therapeutic Targeting from Multiple Angles". Oncotarget 2017 Jan 10, 8(2) 3724-3745. PMCID: PMC5356914.

5. Valentina Minieri, Marco De Dominici, Patrizia Porazzi, Samanta A. Mariani, Orietta Spinelli, Alessandro Rambaldi, Luke F. Peterson, Pierluigi Porcu, **Marja T. Nevalainen**, and Bruno Calabretta. Targeting STAT5 or STAT5-regulated pathways suppresses

leukemogenesis of Ph+ acute lymphoblastic leukemia. Cancer Research (AACR), 2019 Aug 28;78(20):5793-5807. PMID30154155.

6. Maranto C, Udhane V, Hoang DT, Gu L, Alexeev V, Malas K, Cardenas K, Brody JR, Rodeck U, Bergom C, Iczkowski KA, Jacobsohn K, See W, Schmitt SM, **Nevalainen MT**. Stat5a/b Inhibition Sensitizes Prostate Cancer to Radiation through Inhibition of Rad51 and DNA Repair. Clinical Cancer Res. 2018; 24(8):1917-1931.

7. Bassem R. Haddad, Andrew Erickson, Vindhya Udhane, Peter LaViolette, Janice D. Rone, Markku Kallajoki, William See, Antti Rannikko, Tuomas Mirtti, **Marja T. Nevalainen**. Positive STAT5 Protein and Locus Amplification Status Predicts Prostate Cancer Recurrence After Radical Prostatectomy to Assist Precision Medicine of Prostate Cancer. Cancer Epidemiology, Biomarkers and Prevention. 2019 Oct;28(10):1642-1651.

8. Vindhya Udhane, Cristina Maranto, David T. Hoang, Lei Gu, Andrew Erickson, Savita Devi, Pooja G. Talati, Anjishnu Banerjee, Kenneth Iczkowski, Kenneth Jacobsohn, William See, Tuomas Mirtti, Deepak Kilari, **Marja T. Nevalainen**. Enzalutamide-Induced Feed-Forward Signaling Loop Promotes Therapy-Resistant Prostate Cancer Growth Providing an Exploitable Molecular Target for Jak2 Inhibitors. Molecular Cancer Therapeutics (AACR). 2020 Jan;19(1):231-246.

9. William A Hall, Lavannya Sabharwal, Vindhya Udhane, Cristina Maranto, **Marja T Nevalainen**. Cytokines, Jak-Stat Signaling and Radiation-Induced DNA Repair in Solid Tumors: Novel Opportunities for Radiation Therapy. Int. J. Biochemistry and Cell Biology, Medicine-In-Focus, 2020 Aug 19 127:105827. PMID32822847.

10. Maranto C, Udhane V, Jing J, Verma RS, Fahrenkamp D, Muller-Newen G, LaViolette PS, Pereckas M, Sabharwal L, Terhune S, Pattabiraman N, Njar VCO, Imig JD, Wang L, **Nevalainen MT**. Prospects for clinical development of Stat5 inhibitor IST5-002: High transcriptomic specificity in prostate cancer and low toxicity *in vivo.* Cancers (Basel)*,* 2020. Nov18;12(11):3412.doi.10.3390/cancers12113412.

11. Yunguang Sun, Ning Yang, Fransiscus E. Utama , Sameer S. Udhane, Junling Zhang, Amy R. Peck, Alicia Yanac, Katherine Duffey, John F. Langenheim, Vindhya Udhane, Guanjun Xia, Jess F. Peterson, Julie M. Jorns, **Marja T. Nevalainen,** Romain Rouet, Peter Schofield, Daniel Christ, Christopher J. Ormandy, Anne L. Rosenberg, Inna Chervoneva, Shirng-Wern Tsaih, Michael J. Flister, Serge Y. Fuchs, Kay-Uwe Wagner, Hallgeir Rui. NSG-Pro mouse model for uncovering resistance mechanisms and unique vulnerabilities in human luminal breast cancers. Science Advances, 2021 Sep 17; 7(38):eabc8145. Doi:10.1126/sciadv.abc8145. PMCID: PMC8443188.

12. Beinhoff P, Maranto C, Udhane V, Sabharwal L, See W, Jacobsohn K, Iczkowski K, Hall W, Kilari D, **Nevalainen MT.** Second-Generation Jak2 Inhibitors for Advanced Prostate Cancer: Are We Ready for Clinical Development? Invited Review, Cancers (Basel), 2021 Oct 17; 13(20):5204. PMCID: PMC8533841

13. William A Hall, Mandana Kamgar, Beth A Erickson, Sarah Beltrán Ponce, Susan Tsai, **Marja T Nevalainen**, Kathleen K Christians, Ben George, Kulwinder S Dua, Abdul H Khan, Douglas B Evans, Asfar S Azmi. Updates and New Directions in the Use of Radiation Therapy for the Treatment of Pancreatic Adenocarcinoma: Dose, Sensitization, and Novel Technology. Cancer and Metastasis Reviews, 2021 Oct 6. Doi: 10.1007/s10555-021-0993-z. PMID: 34611794.

14. Maranto C*, Udhane VU*, Sabharwal L*, Pitzen S, McCluskey B, Devi S, Johnson S, Jacobsohn K, Banerjee A, Iczkowksi KA, Wang L, Dehm S, Nevalainen MT. Stat5 induces androgen receptor (AR) gene transcription in prostate cancer and offers a druggable pathway to target androgen receptor signaling. In Revision, Science Advances, 2023.