

Nathan Lack

University of British Columbia, Canada • nlack@prostatecentre.com

SCIENTIFIC EXPERIENCE

VANCOUVER PROSTATE CENTRE, Vancouver, Canada

Aug 2017 – Present

Senior Research Scientist

- Assistant Professor in Faculty of Medicine at the University of British Columbia.
- Co-director of the VPC Drug Design and Pharmacology core.
- Research program focused on study characterizing androgen receptor and HOXB13 mechanism of action in aggressive prostate cancer.
- Characterized epigenetic modifying enzymes as a mechanism of therapeutic resistance.

KOÇ UNIVERSITY SCHOOL OF MEDICINE, Istanbul, Turkey

Aug 2011 - Present

Assistant/Associate Professor

- Founded an androgen receptor laboratory at one of the leading university in Turkey with a focus on developing innovative functional genomic techniques to study prostate cancer.
- Developed the undergraduate molecular biology and biochemistry education program.

VANCOUVER PROSTATE CENTRE, Vancouver, Canada

Nov 2009 – July 2011

Postdoctoral Fellow with Professors Paul Rennie, Art Cherkasov and Emma Guns

- Identified and characterized novel androgen receptor inhibitors using *in silico* screening combined with biochemical and cell-based high-throughput assays.
- Awarded the Michael Smith Foundation for Health Research Postdoctoral Fellowship.

ANORMED INC., Langley, Canada

May 2003 - Jan 2004

Scientific Assistant, Pharmacology

- Planned, organized and executed pre-clinical and clinical toxicology and pharmacokinetic studies to support FDA submission of AMD3100/Plerixafor.

EDUCATION

UNIVERSITY OF OXFORD

Doctor of Philosophy in Pharmacology with Professor Edith Sim

Oct 2005 - Oct 2009

- Identified, expressed and characterized a hydrolytic enzyme involved in cholesterol metabolism as a novel drug target against *Mycobacterium tuberculosis*.
- Received the Natural Science and Engineering Research Council of Canada Postgraduate Scholarship

UNIVERSITY OF BRITISH COLUMBIA

Bachelor of Science, Microbiology and Immunology

Sept 1999 - May 2004

- Conducted research with Professor Wilf Jefferies to characterize TAP-dependent antigen presentation in cancerous cells.

TEACHING

KOÇ UNIVERSITY SCHOOL OF MEDICINE, Istanbul, Turkey

Aug 2011 - Present

Assistant/Associate Professor

- Taught molecular biology and biochemistry to undergraduate medical students.
- Ranked in the top 5% of all faculty by students.

UNIVERSITY OF OXFORD, Oxford, United Kingdom
St. Peters/New/Queens College Tutor

Nov 2005 – Sep 2009

- Taught biochemistry and molecular biology to Oxford chemistry, biochemistry and medical students.

NAL TUTORING, Vancouver, Canada
Founder and Director

Mar 2004 - May 2005

- Created, organized, and ran an independent tutoring business that taught biochemistry, immunology and medical microbiology to over 800 first- and second-year students from the University of British Columbia.

PUBLICATIONS

Özgün F, Kaya Z, Morova T, Geverts B, Abraham TE, Houtsmuller AB, van Royen ME, **Lack NA**. (2021) *DNA binding alters ARv7 dimer interactions*. J Cell Sci. Jul 15;134(14).

Huang CF, Lingadahalli S, Morova T, Ozturan D, Hu E, Yu IPL, Linder S, Hoogstraat M, Stelloo S, Sar F, van der Poel H, Altintas UB, Saffarzadeh M, Le Bihan S, McConeghy B, Gokbayrak B, Feng FY, Gleave ME, Bergman AM, Collins C, Hach F, Zwart W, Emberly E, **Lack NA**. (2021) *Functional mapping of androgen receptor enhancer activity*. Genome Biol. May 11;22(1):149.

Morova T, Gonen M, Uyulur F, Gursoy A, Keskin O, **Lack NA**. (2020) *Androgen receptor binding sites are highly mutated in prostate cancer*. Nat Commun. Feb 11;11(1):832.

Saraç H, Morova T, Pires E, McCullagh J, Kaplan A, Bağcı-Önder T, Önder T, Kawamura A, **Lack NA**. (2020) *Systematic characterization of epigenetic modifying enzymes identifies KDM3B as a key regulator in castration resistant prostate cancer*. Oncogene. 2020 Mar;39(10):2187-2201

Woo G, Fernandez M, Hsing M, **Lack NA**, Cavga AD, Cherkasov A. (2020) *DeepCOP: deep learning-based approach to predict gene regulating effects of small molecules*. Bioinformatics. Feb 1;36(3):813-818

Cato L, de Tribolet-Hardy J, Lee I, Rottenberg JT, Coleman I, Melchers D, Houtman R, Xiao T, Li W, Uo T, Sun S, Kuznik NC, Göppert B, Ozgun F, van Royen ME, Houtsmuller AB, Vadhi R, Rao PK, Li L, Balk SP, Den RB, Trock BJ, Karnes RJ, Jenkins RB, Klein EA, Davicioni E, Gruhl FJ, Long HW, Liu XS, Cato ACB, **Lack NA**, Nelson PS, Plymate SR, Groner AC, Brown M. (2019) *ARv7 Represses Tumor-Suppressor Genes in Castration-Resistant Prostate Cancer*. Cancer Cell. Mar 18;35(3):401-413

Quigley DA, Dang HX, Zhao SG, Lloyd P, Aggarwal R, Alumkal JJ, Foye A, Kothari V, Perry MD, Bailey AM, Playdle D, Barnard TJ, Zhang L, Zhang J, Youngren JF, Cieslik MP, Parolia A, Beer TM, Thomas G, Chi KN, Gleave M, **Lack NA**, Zoubeidi A, Reiter RE, Rettig MB, Witte O, Ryan CJ, Fong L, Kim W, Friedlander T, Chou J, Li H, Das R, Li H, Moussavi-Baygi R, Goodarzi H, Gilbert LA, Lara PN Jr, Evans CP, Goldstein TC, Stuart JM, Tomlins SA, Spratt DE, Cheetham RK, Cheng DT, Farh K, Gehring JS, Hakenberg J, Liao A, Febbo PG, Shon J, Sickler B, Batzoglou S, Knudsen KE, He HH, Huang J, Wyatt AW, Dehm SM, Ashworth A, Chinnaiyan AM, Maher CA, Small EJ, Feng FY. (2018) *Genomic Hallmarks and Structural Variation in Metastatic Prostate Cancer*. Cell. 2018 Jul 26;174(3):758-769

Dalal K, Morin H, Ban F, Shepherd A, Fernandez M, Tam KJ, Li H, LeBlanc E, **Lack NA**, Prinz H, Rennie PS, Cherkasov A. (2018) *Small molecule-induced degradation of the full length and V7 truncated variant forms of human androgen receptor*. Eur J Med Chem. Sep 5;157:1164-1173.

Can F, Menekse S, Ispir P, Atac N, Albayrak O, Demir T, Karaaslan DC, Karahan SN, Kapmaz M, Kurt Azap O, Timurkaynak F, Simsek Yavuz S, Basaran S, Yoruk F, Azap A, Koculu S, Benzonana N, **Lack NA**, Gönen M, Ergonul O. (2018) *Impact of the ST101 clone on fatality among patients with colistin-resistant Klebsiella pneumoniae infection*. J Antimicrob Chemother. May 1;73(5):1235-1241

Kurt IC, Sur I, Kaya E, Cingoz A, Kazancioglu S, Kahya Z, Toparlak OD, Senbabaoglu F, Kaya Z, Ozyerli E, Karahüseynoglu S, **Lack NA**, Gümüş ZH, Onder TT, Bagci-Onder T. (2017) *KDM2B, an H3K36-specific demethylase, regulates apoptotic response of GBM cells to TRAIL*. Cell Death Dis. Jun 29;8(6):e2897.

Ryan A, Polycarpou E, **Lack NA**, Evangelopoulos D, Sieg C, Halman A, Bhakta S, Eleftheriadou O, McHugh TD, Keany S, Lowe ED, Ballet R, Abuhammad A, Jacobs WR Jr, Ciulli A, Sim E. (2017) *Investigation of the mycobacterial enzyme HsaD as a potential novel target for anti-tubercular agents using a fragment-based drug design approach*. Br J Pharmacol. 2017 Jul;174(14):2209-2224.

Fineran P, Lloyd-Evans E, **Lack NA**, Platt N, Davis LC, Morgan AJ, Höglinger D, Tatituri RV, Clark S, Williams IM, Tynan P, Al Eisa N, Nazarova E, Williams A, Galione A, Ory DS, Besra GS, Russell DG, Brenner MB, Sim E, Platt FM. (2016) *Pathogenic mycobacteria achieve cellular persistence by inhibiting the Niemann-Pick Type C disease cellular pathway*. Wellcome Open Res. Nov 18;1:18.

Senbabaoglu F, Cingoz A, Kaya E, Kazancioglu S, **Lack NA**, Acilan C, Bagci-Onder T. (2016) *Identification of Mitoxantrone as a TRAIL-sensitizing agent for Glioblastoma Multiforme*. Cancer Biol Ther. Mar 30;17(5):546-57

Oktem O, Bildik G, Senbabaoglu F, **Lack NA**, Akin N, Yakar F, Urman D, Guzel Y, Balaban B, Iwase A, Urman B. (2015) *Cytotoxicity and mitogenicity assays with real-time and label-free monitoring of human granulosa cells with an impedance-based signal processing technology intergrating micro-electronics and cell biology*. Reprod Toxicol. Dec 30;60:82-91.

Acar Ö, Özkurt E, Demir G, Saraç H, Alkan C, Esen T, Somel M, **Lack NA**. (2015) *Determining the origin of synchronous multifocal bladder cancer by exome sequencing*. BMC Cancer. Nov 9;15:871.

Kucuk C, Jiang B, Hu X, Zhang W, Chan J, Xiao W, **Lack NA**, Alkan C, Williams J, Avery K, Kavak P, Scuto A, Sen E, Gaulard P, Staudt L, Iqbal J, Zhang W, Cornish A, Gong Q, Yang Q, Sun H, d'Amore F, Leppä S, Liu W, Fu K, de Leval L, McKeithan T, Chan W. (2015) *Activating mutations of STAT5B and STAT3 in lymphomas derived from $\gamma\delta$ -T or NK cells*. Nat Comm. Jan 14;6:6025.

Evangelopoulos D, Gupta A, **Lack NA**, Maitra A, ten Bokum AMC, Kendall S, Sim E, Bhakta S. (2014) *Characterisation of a putative AraC transcriptional regulator from Mycobacterium smegmatis*. Tuberculosis. Dec;94(6):664-71.

Garipler G, Mutlu N, **Lack NA**, Dunn CD. (2014) *Deletion of conserved protein phosphatases reverses defects associated with mitochondrial DNA damage in Saccharomyces cerevisiae*. PNAS. Jan 28;111(4):1473-8.

Lack NA*, Li H*, Hassona MD*, Axerio-Cilies P, Leblanc E, Tavassoli P, Kanaan N, Frewin K, Singh K, Adomat H, Böhm KJ, Prinz H, Guns ET, Rennie PS, Cherkasov A. (2013) *Characterization of a new class of androgen receptor antagonists with potential therapeutic application in advanced prostate cancer*. Mol Cancer Ther. Nov;12(11):2425-35 * Co-first author

Acar O, Esen T, **Lack NA**. (2013) *New therapeutics to treat castrate-resistant prostate cancer*. ScientificWorldJournal. May 27;2013:379641.

Bowdish DME, Sakamoto K, **Lack NA**, Hill PC, Sirugo G, Newport M, Gordon S, Hill AVS, Vannberg FO. (2013) *Genetic variants of MARCO are associated with susceptibility to pulmonary tuberculosis in a Gambian population*. BMC Med Genet. Apr 23;14:47.

Munuganti RS, Leblanc E, Axerio-Cilies P, Labriere C, Frewin K, Singh K, Hassona MD, **Lack NA**, Li H, Ban F, Tomlinson Guns E, Young R, Rennie PS, Cherkasov A. (2013) *Targeting the Binding Function 3 (BF3) Site of the Androgen Receptor Through Virtual Screening. 2. Development of 2-((2-phenoxyethyl) thio)-1H-benzimidazole Derivatives*. J Med Chem. Feb 14;56(3):1136-48.

Singh N, Halliday AC, Knight M, **Lack NA**, Lowe E and Churchill GC. (2012) *Cloning, expression, purification, crystallisation and X-ray analysis of inositol monophosphatase from Mus musculus and Homo sapiens*. Acta Crystallogr Sect F Struct Biol Cryst Commun. Oct ;68(Pt 10):1149-52.

Basha G, Omilusik K, Chavez-Steenbock A, Reinicke AT, **Lack N**, Choi KB, Jefferies WA. (2012) *A CD74-dependent MHC class I endolysosomal cross-presentation pathway*. Nat Immunol. Feb; 13(3):237-245.

Lack NA, Axerio-Cilies P, Tavassoli P, Han FQ, Chan KH, LeBlanc E, Guns E, Guy RK, Rennie P and Cherkasov A. (2012) *Targeting the Binding Function 3 (BF3) Site of the Human Androgen Receptor Through Virtual Screening*. J Med Chem. Dec; 54(24):8563-73.

Lack NA*, Axerio-Cilies P*, Shashi Nayana MR, Chan KH, Yeung A, LeBlanc E, Guns E, Rennie P and Cherkasov A. (2011) *Inhibitors of androgen receptor activation function-2 (AF2) site identified through virtual screening*. J Med Chem. Sep; 54(18): 6197-205. *Co-first author

Abuhammad A, **Lack N**, Schweichler J, Staunton D, Sim RB, Sim E. (2011) *Improvement of the expression and purification of Mycobacterium tuberculosis arylamine N-acetyltransferase (TBNAT) a potential target for novel anti-tubercular agents*. Protein Expr. Purif. Dec; 80(2): 246-52.

Abdelbaqi K, **Lack NA**, Guns E, Kotha L, Safe SJ, Sanderson T. (2011) *Antiandrogenic and growth inhibitory effects of ring-substituted analogs of 3,3'-diindolylmethane (ring-DIMs) in hormone-responsive LNCaP human prostate cancer cells*. Prostate. Sep; 71(13):1401-12.

Lack NA, Yam KC, Lowe ED, Horsman GP, Owen R, Sim E, Eltis LD. (2010) *Characterization of a C-C hydrolase from Mycobacterium tuberculosis involved in cholesterol metabolism*. J Biol Chem. Jan; 285(1): 434-43.

Carroll MV, **Lack N**, Sim E, Sim RB. (2009) *Multiple routes of complement activation by Mycobacterium bovis BCG*. Mol Immuno. Oct; 46(16): 3367-78.

Lack NA, Kawamura A, Fullam E, Laurieri N, Beard S, Russell AJ, Evangelopoulos D, Westwood I, Sim E. (2009) *Temperature stability of proteins essential for the intracellular survival of Mycobacterium tuberculosis*. Biochem J. Mar; 418(2): 369-78.

Sim E, **Lack N**, Wang CJ, Long H, Westwood I, Fullam E, Kawamura A. (2008) *Arylamine N-acetyltransferases: structural and functional implications of polymorphisms*. Toxicology. Dec; 254(3): 170-83.

Lack NA, Lowe ED, Liu J, Eltis LD, Noble ME, Sim E, Westwood IM. (2008) *Structure of HsaD, a steroid-degrading hydrolase, from Mycobacterium tuberculosis*. Acta Crystallogr Sect F Struct Biol Cyst Commun. Jan; 64(Pt 1): 2-7.

Sim E, Sandy J, Evangelopoulos D, Fullam E, Bhakta S, Westwood I, Krylova A, **Lack N**, Noble M. (2008) *Arylamine N-acetyltransferases in mycobacteria*. Curr Drug Metab. Jul; 9(6): 510-9.

Wakefield L, Long H, **Lack NA**, Sim E. (2007) *Ocular defects associated with a null mutation in the mouse arylamine N-acetyltransferase 2 gene*. Mamm Genome. Apr; 18(4): 270-6.

Lack NA, Green B, Dale DC, Calandra GB, Lee H, MacFarland RT, Badel K, Liles WC, Bridger GA. (2005) *A Pharmacokinetic/Pharmacodynamic Model for the Mobilization of CD34+ Hematopoietic Progenitor Cells by AMD3100*. Clin Pharmacol Ther. May; 77(5): 427-36.

PRE-PRINT

Yedier-Bayram O, Gokbayrak B, Aksu AC, Cavga AD, Kayabolen A, Kala EY, Karabiyik G, Günsay R, Morova T, Uyulur F, **Lack NA**, Önder TT, Bagci-Onder T. (2021) *EPIKOL, a chromatin-focused CRISPR/Cas9-based screening platform, to identify cancer-specific epigenetic vulnerabilities*. doi.org/10.1101/2021.05.14.444239

Baca SC, Singler C, Zacharia S, Seo JH, Morova T, Hach F, Ding Y, Schwarz T, Huang CCF, Kalita C, Groha S, Pomerantz MM, Wang V, Linder S, Sweeney CJ, Zwart W, **Lack NA**, Pasaniuc B, Takeda DY, Gusev A, Freedman ML. (2021) *Genetic determinants of chromatin reveal prostate cancer risk mediated by context-dependent gene regulation*. doi.org/10.1101/2021.05.10.443466

Kayabolen A, Akcan U, Ozturan D, Sarayloo E, Nurtop E, Ozer B, Sahin GN, Dogan O, **Lack NA**, Kaya M, Albayrak Cem, Can F, Solaroglu I, Bagci-Onder T. (2021) *Protein scaffold-based multimerization of soluble ACE2 efficiently blocks SARS-CoV-2 infection in vitro*. doi.org/10.1101/2021.01.04.425128

Zhang F, Wong S, Lee J, Lingadahalli S, Wells C, Saxena N, Sanchez C, Sun B, Parra-Nuñez AK, Chan N, Bui JM, Wang Y, Rennie PS, Lack NA, Cherkasov A, Gleave M, Gsponer J, Lallous N (2021). *Dynamic phase separation of the androgen receptor and its coactivators to regulate gene expression*. doi.org/10.1101/2021.03.27.437301

BOOK CHAPTERS

Sarac H, Cherkasov A, **Lack NA**. Development of novel androgen receptor inhibitors to overcome castrate resistant prostate cancer, *Advancing Approaches to overcoming cancer drug resistance*, 1st Edition, (2020) Editors: Franco Vizzecoumar and Andrew Freywald

Lack NA, Leygue E. Chapter 20: Hormones and Cancer, *The Basic Science of Oncology*, 6th Edition (2020) , Editors: Lea Harrington, Ian Tannock, Richard Hill, Dave Cescon

PATENTS

BINDING FUNCTION3 (BF3) SITE COMPOUNDS AS THERAPEUTICS AND METHODS FOR THEIR USE: WO2015154169A1 - **Licensed**

TREATMENT OF LYSOSOMAL DISORDERS (ANTI-TNF THERAPY):
PCT/GB2015/051980

INHIBITORS OF ANDROGEN RECEPTOR ACTIVATION FUNCTION-2 (AF2) AS THERAPEUTICS AND METHODS FOR THEIR USE: WO 2013023300 A1

A CELL PERMEANT AND POTENT INHIBITOR OF IMPASE: PATENT APPLICATION NUMBER 0922058.3 – **Licensed**

ADMINISTRATIVE

- Co-director of Drug development core at Vancouver Prostate Centre (2017-present)
- Director of Bioinformatics and Microscopy core facilities at Koç University (2015-2017)
- Founder and co-Director of Laboratories at the School of Medicine (2013-2017)
- Member of School of Medicine Faculty search committee (2015-2017)

RESEARCH GRANTS

Koç University

Marie Curie Integration Grant, Principle Investigator (2012-2015) – \$105,000

ISTKA Developmental Grant, Co-Investigator (2013-2014) – \$1,020,000

TUBITAK 3501, Principle Investigator (2013-2016) – \$98,000

TUBITAK 1002, Principle Investigator (2014-2015) – \$10,000

TUBITAK 1001, Principle Investigator (2014-2017) – \$145,000

TUBITAK 1001, Principle Investigator (2015-2018) – \$169,000

Newton Advanced Fellowship, Principle Investigator (2015-2018) – \$220,000

Koç University Seed Funding, Principle Investigator (2015-2017) – \$12,000

TUBITAK 1003, Co-Investigator (2016-2019) – \$1,100,000

TUBITAK 1003, Co-Investigator (2017-2020) – \$1,100,000

TUBITAK 1001, Principle Investigator (2019-2022) - \$129,000

Vancouver Prostate Centre

CIHR Project Grant, Principle Investigator (2018-2020) - \$350,000

CIHR Project Grant, Co-Investigator (2018-2021) - \$450,000

CIHR Project Grant , Principle Investigator (2020-2023) - \$449,000

PCC Discovery Grant, Co-Investigator (2019-2022) - \$250,000

Department of Defense, Co-Principle Investigator (2021-2024) - \$940,000

INDUSTRY FUNDING

- Identification and characterization of novel epigenetic modifying enzymes in late-stage prostate cancer, AstraZeneca (2016-2021)
- Development of a SBMA reporter cell line, Nido Bioscience (2019-2021)
- Impact of polyQ expansion on AR co-regulatory network, Nido Bioscience (2021-2022)

PROFESSIONAL SOCIETIES

- American Association for Cancer Research
- International Society for the Study of Xenobiotics
- British Society of Pharmacology
- Lifescience British Columbia

AWARDS AND HONOURS

- Turkish Science Academy – Young Scientists Award (2020)
- PacRim meeting - Early Career Award (2019)
- TUBA GEBIP- Top Young National Scientist (2017)
- VCHRI - Rising Star Scientific Award (2011)
- Lorne Sullivan - Best Basic Science Research Award (2010)