BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Kye Stachowski, PhD**

eRA COMMONS USERNAME (credential, e.g., agency login): **STACHOWSKI7**

POSITION TITLE: **Research Fellow**

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
Purdue University, West Lafayette, IN	B.S.	05/2016	ACS Chemistry
The Ohio State University, Columbus, OH	Ph.D.	08/2021	Structural Biology
Cincinnati Children's Hospital, Cincinnati, OH	Postdoc	Present	Structural Biology

A. Personal Statement

My long-term research goal is to develop novel therapeutics through mechanistic studies of protein/enzyme targets in human disease. My academic training and research experience have provided me with the foundations in structural biology, biochemistry, biophysics, and molecular biology. As an undergraduate at Purdue University, I was privileged to participate in research with Dr. Jo Ann Banks uncovering sex regulation mechanisms in ferns, before moving to graduate school at OSU where I studied under Dr. Mark P. Foster. As a graduate student, I used various structural biology techniques including nuclear magnetic resonance and cryo-electron microscopy to elucidate enzyme autoinhibition, assembly, and activation mechanisms that resulted in multiple publications. I have received multiple awards for communication efforts in various scientific forums during my time in graduate school.

For my postdoctoral training, I will continue to forge my long-term research goal by partaking in structural and biochemical studies addressing a novel leukemia therapeutic. My sponsor, Dr. Nicolas Nassar, is a well-recognized researcher with expertise in drug development, structural biology, and patient derived/mouse models of leukemia. My postdoctoral research will provide new conceptual and technical skills while cementing my foundational skills acquired during graduate school. In addition to the research experience, my Ruth L. Kirschstein National Research Service Award will provide multiple opportunities for professional development, research communications, and exposure to therapeutic intellectual property.

B. Positions, Scientific Appointments, and Honors

Positions

2021 – Pres. Research Fellow, Cincinnati Children's Hospital Medical Center

Appointments and Memberships

2020 – 2021 Ohio State University College of Arts and Sciences Dean's Student Advisory Board (Appointed)
2019 – 2021 Ohio State University Council of Graduate Students (Elected)
2020 American Association for the Advancement of Science (Member)

Honors and Awards

2021 – Pres. Ruth L. Kirschstein National Research Service Award (T32)
2021 Ohio State University Center for Electron Microscopy Micrograph Competition – 1st Place
2021 Molecular Biophysics Training Program Symposium – Best Trainee Talk
2019 Dow Chemical Corp. – 1st Place Poster Presentation Award

C. Contributions to Science

1. Early Career

My early career research focused on using molecular biology methods to silence genes to further understand how vascular plants differentiate their sex. Here, I designed, produced, and tested 18 RNAi constructs used to silence genes. These genetic mutants were assayed to study the effects of abscisic acid on the sexual differentiation pathway of the fern *Ceratopteris richardii.* We found that abscisic acid originally controlled plant stomata in relation to dormancy and then pathways evolved to be used to in sexual differentiation.

McAdam, S. A. M., Brodribb, T. J., Banks, J. A., Hedrich, R., Atallah, N. M., Cai, C., Geringer, M. A., Lind, C., Nichols, D. S., **Stachowski, K**., Geiger, D., & Sussmilch, F. C. (2016). Abscisic acid-controlled sex before transpiration in vascular plants. *Proceedings of the National Academy of Sciences of the United States of America*, *113*(45), 12862–12867. PMID: 27791082

2. Graduate Career

My graduate career research focused on using structural biology techniques, backed up by experimental and computational biochemical experiments to elucidate the function of macromolecules including enzymes, proteins, and cyclic peptides. Results from these works furthered our understanding of how cyclic peptides are structured (or unstructured), how the binding of ligands to a polyvalent protein confer allosteric communication, and how assembly of large macromolecular complexes can result in enzymatic activity.

Stachowski, K., Wen, J., Liao, H., Hempfling, J. P., Qian, Z., Yuan, C., Foster, M. P., & Pei, D. (2020). Rational design of cell-permeable cyclic peptides containing a D-Pro-L-Pro motif. *Bioorganic and Medicinal Chemistry*, *28*(20), 115711. PMID: 33069067

Unnikrishnan, A., Amero, C., Yadav, D. K., **Stachowski, K**., Potter, D., & Foster, M. P. (2020). DNA binding induces a cis-to-trans switch in Cre recombinase to enable intasome assembly. *Proceedings of the National Academy of Sciences of the United States of America*, *117*(40), 24849–24858. PMID: 32968014

Stachowski, K., Norris, A. S., Potter, D., Wysocki, V. H., & Foster, M. P. (2022). Mechanisms of Cre recombinase synaptic complex assembly and activation illuminated by Cryo-EM. *Nucleic Acids Research*, *50*(3), 1753–1769. PMID: 35104890

Phan, H. D., Norris, A. S., Du, C., **Stachowski, K**., Foster, M. P., Wysocki, V. H., Gopalan, V. (2022). Use of native mass spectrometry and mass photometry to elucidate structure-function relationships in Methanocaldococcus jannaschii RNase P, a multi-subunit catalytic ribonucleoprotein. *In press.*

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
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NAME: **Nicolas N. Nassar, PhD**

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

POSITION TITLE: **Associate Professor**

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
Ingénieurs Electriciens de Grenoble/France	Engineer	07/1987	Applied Physics
EMBL, Grenoble/France	Ph.D.	10/1992	Protein Crystallography
Institut Jean-Pierre Ebel, Grenoble/France	Postdoc	1992-1993	Protein Crystallography
Max-Planck-Institut, Dortmund/Germany	Postdoc	1993-1996	Structural Biology

A. Personal Statement

My training is in structural biology. Research in my laboratory at Cincinnati's Children Hospital Medical Center (CCHMC) focuses on the signaling of the RAS and RHO families of small GTP-binding proteins and of the UBASH3A/B family of protein tyrosine phosphatases (PTPs). I am particularly interested in the protein-protein interactions these proteins make. My laboratory has, over the past 20 years, made a number of significant and original contributions to the molecular understanding of key players in both families using structural, biochemical, and cellular approaches. I was the first to show how RAS interacts with a downstream effector and with a GAP and to describe a novel 'open non-signaling conformation' of RAS. My laboratory was the first to show that UBASH3B is a PTP and to determine its mechanism of hydrolysis and its three-dimensional structure. To develop new therapeutics that improve outcome for pediatric patients, I became interested in identifying small molecule inhibitors of RAS/RAC proteins. My laboratory has the necessary biochemical, biophysical, cellular, and *in vivo* animal model expertise to conduct the proposed mechanistic studies.

My laboratory has developed the small molecule compound IODVA1 (Gasilina *et al., PLoS One* 2020; Hegde *et al., Leukemia* 2021) with inhibitory activity in cellular and mouse models of pediatric patient-derived xenograft leukemia including TKI-resistant leukemia and in cellular and mouse models of breast and lung cancers. IODVA1 is a first-in-class inhibitor of VAV3, a RAC activator. This small molecule technology has been recently patented at our institution. My research is now geared towards testing the efficacy of IODVA1 in various cancer models where VAV3 is a target with the goal of initiating a clinical trial at our institution.

I would like to draw attention to the following ongoing support and patents:

- R01 CA237016 (Nassar, PI) 07/01/20-06/30/24
NCI
Targeted Inhibition in Leukemia

- iAward (Nassar, PI) 02/01/21-01/31/22
SANOFI
Targeted Inhibition in Cancer

Patents:

Application N°: 11/496959 Filing Date: 07/31/2006
Title: GTPase Inhibitors and Methods of Use and Crystal Structure of RAC1 GTPase
Inventors: Zheng, Yi; Nassar, Nicolas; Skowronek, Karlheinz R.

Application N°: 62/652,464 Filing Date: 04/04/2020
Title: Targeted Inhibition of Vav3/Rac in Leukemia and other Neoplasia
Inventor: Nassar, Nicolas; Gasilina, Anjelika; Seibel, William; Cancelas, Jose.

B. Positions, Scientific Appointments, and Honors

Positions and Employments

12/21 – present: Director, Proton Research Facility, Cincinnati Children's Hospital, Liberty Township, Ohio.
09/21 – present: Research Member in Basic Science Program, University of Cincinnati Cancer Centre.
12/20 - present: Associate Professor affiliated with the Department of Molecular Genetics and Biochemistry, University of Cincinnati.
09/10 - present: Associate Professor, Division of Experimental Hematology and Cancer Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH
06/07 – 09/10: Research Assistant Professor, Department of Physiology & Biophysics, Stony Brook University, NY
05/00 – 05/07: Assistant Professor, Department of Physiology & Biophysics, Stony Brook University, NY.
11/96 – 04/00: Research Associate, Department of Molecular Medicine, Cornell, Ithaca NY (Supervisor: Dr. Rick Cerione)

Other Experience and Professional Memberships

2021 – present: Editorial Board Member, Current Oncology, MDPI
2021 – present Ad hoc reviewer, Developmental Therapeutics (DT) study section, NCI
2021 – present Ad hoc reviewer, SCORE study section, NIGMS
2019 - 2021 Ad hoc reviewer, NCI Special Emphasis Panel
2010-2018 Member of the grant-review panel, Breast Cancer 'Cell Biology', Department of Defense
2014-2017 Member of the grant-review panel, American Heart Associate, Study Section 'Physical Chemistry'
2014-2016 Reviewer, UC Cancer Center Pilot Program
2013 Reviewer, The Netherlands Organization for Scientific Research
2011-2012 Reviewer, Marlene Harris-Ride Cincinnati Breast Cancer Pilot Program
2011 Reviewer, Graduate Women in Science.
2010 *Ad Hoc* Reviewer for the Susan G. Komen.
2008-2010 Member of the grant-review panel, Breast Cancer Drug Development, Department of Defense.
2007-2010 Member of the proposal review panel (PRP) for Brookhaven National Laboratory (Upton, NY) for macromolecular crystallography.
2008 Reviewer, Targeted Research Opportunity, Stony Brook University
2005 Reviewer, The Philip Morris Research Management Group
2005 Reviewer, Louisiana Board of Regents support fund

Honors

1987–1990: French Ministry of Education Fellowship Award.
1993–1996: ONYX Pharmaceuticals Fellowship.

C. Contributions to Science

1. During my graduate training as a structural biologist (EMBL, Dr. Stephen Cusack), my research focused on the crystal structure of the *E. coli* Serine aminoacyl-tRNA synthetase (SerRS). AARSs are essential enzymes that charge their specific tRNAs (i.e. ^{Ser}tRNAs) with its cognate amino acid (i.e. Ser) and therefore are essential for the specificity of the genetic code and proper translation. They are believed to be among the first enzymes linking codons to amino acids. Before we solved the SerRS, all known structures of AARSs (e.g. MetRS, TrpRS) shared the classical Rossmann-fold. However, sequence motifs specific for this fold were absent in the SerRS primary structure. The three-dimensional structure showed that SerRS had a new

fold and a novel ATP-binding site that was distinct from the Rossman-fold. This was the first step towards dividing the 20 AARSs into two distinct families. Subsequent AARS structures confirmed the fold we identified. Our work was published in *Nature* with a *News and Views* introduction 'Synthetase with a difference'.

a) Stephen Cusack, Carmen Berthet-Colominas, Michael Härtlein, **Nicolas Nassar**, Reuben Leberman "A second class of synthetase structure revealed by X-ray analysis of *Escherichia coli* seryl-tRNA synthetase at 2.5 Å" *Nature* **347**, 249-255 (1990). PMID: 2205803

b) **Nicolas Nassar** "Crystal Structure of the E. coli tRNA synthetase at 2.5 Å resolution", PhD Thesis, University Joseph Fourier, Grenoble/France.

c) Cusack, S., Berthet-Colominas, C., Biou, V., Borel, F., Fujinaga, M., Hartlein, M., **Nassar, N**., Price, S., Tukalo, A., Yaremchuk, D., Leberman, R. (1993) "The crystal structure of the seryl-tRNA synthetase and its complexes with ATP and tRNASer" In The translational Apparatus: eds. Nierhaus, K.H., Fanceschi, F., Subramian, A.P., Erdmann, V.A. & Wittmann-Liebold, B., Plenum Press, New York, pp 1-12.

2. During my postdoctoral work at the Max-Plank Institut (Heidelberg & Dortmund/Germany, Dr. Alfred Wittinghofer), I switched to studying Ras signaling. I was the first to show how Ras interacts with its downstream effector Raf-kinase by solving the crystal structure of GTP-bound Rap in complex with the Ras-binding domain of Raf (RafRBD). This structure was published in *Nature* and is the hallmark of how Ras binds to its effectors. To understand the differences between Ras and Rap binding to RafRBD, I mutated two residues on Rap and showed that these were enough to bring the affinity to RafRBD closer to that of Ras. This paper was published in *Nature Structural Biology* with a *News and Views* by Frank McCormick (UCSF). It was also featured on the cover. I was also involved in the crystal structure of RCC1, the guanine exchange factor of the nuclear trafficking regulator Ran.

a) **Nicolas Nassar,** Gudrun Horn, Christian Herrmann, Anna Scherer, Franck McCormick, Alfred Wittinghofer. "The 2.2 Å crystal structure of the Ras-binding domain of the serine/threonine kinase c-Raf1 in complex with Rap1A and a GTP analogue" *Nature* **375**, 554 - 560 (1995). PMID: 7791872

b) Christoph Block, Ralf Janknecht, Christian Herrmann, **Nicolas Nassar**, Alfred Wittinghofer "Quantitative structure-activity analysis correlating Ras/Raf interaction *in vitro* to Raf activation *in vivo*" *Nat. Struct. Biol.* **3**, 244-251 (1996). PMID: 8605626

c) **Nicolas Nassar**, Gudrun Horn, Christian Herrmann, Christoph Block, Ralf Janknecht, Alfred Wittinghofer. "Ras/Rap effector specificity determined by charge" *Nat. Struct. Biol.* **3**, 723-729 (1996). PMID: 8756332

d) Alfred Wittinghofer and **Nicolas Nassar**. "How Ras-related proteins talk to their effectors" *TIBS* **21**, 488-491 (1996). PMID: 9009833

3. During my stay at Cornell University (Department of Molecular Medicine, Dr. Rick Cerione), I showed using X-ray crystallography how the small GTP-binding protein Cdc42 interacts with its GTPase Activating Protein (GAP), and how GAP accelerates GTP-hydrolysis by constraining the dynamics of the switch loops on Cdc42 and introducing an Arg-finger close to the γP. I also contributed to solving the crystal structure of the prenylated-Cdc42 in complex with another regulator, the guanine dissociation inhibitor (GDI). This structure was a tour de force because it featured the first structure of a geranyl-geranylated GTPase and showed how the GDI solubilizes it from the plasma membrane. This work featured the cover of *Cell*.

a) Hoffman, G.R., **Nassar, N**., Oswald, R.E, Cerione, R.A. "Fluoride Activation of the Rho family GTP-binding protein Cdc42Hs" *J. Biol. Chem.* **273**, 4392-4399 (1998). PMID: 9468490

b) **Nicolas Nassar**, Gregory R. Hoffman, Danny Manor, Jon C. Clardy, Richard Cerione "Structures of Cdc42 bound to the active and catalytically compromised forms of the Cdc42GAP" *Nat. Struct. Biol*. **5**, 1047-1052 (1998). PMID: 9846874

c) Gregory R. Hoffman, **Nicolas Nassar**, Rick Cerione "Structure of the Rho family GTP-binding protein Cdc42 in complex with the multifonctional regulator RhoGDI" *Cell* **100**, 345-356 (2000). PMID: 10676816

4. As an independent investigator, I followed up on my previous work on small G-proteins. I was interested in how the dynamics of RAS switch loops are essential for its proper signaling. I adopted a mutagenesis approach combined with biochemical and cellular studies. I focused on the conserved ^{57}DTAG^{60} motif, which is essential for the transition between the RAs active and inactive states. I characterized the Ala59 to Gly (A59G) mutation and showed that the structure of this RAS mutant mimics that of a transition state adopted by RAS along the path of GTP-hydrolysis (going from the active state or GTP-bound to the inactive state or

GDP-bound state) and is similar to that of a structure described in a targeted molecular dynamics study by M. Karplus (Ma & Karplus, 1995). Similarly, we characterized the G60A mutant of RAs and showed that in the GTP-bound form, this mutant adopts the 'open conformation' similar to nucleotide free RAs in complex with SOS1. Targeting the structure of this mutant led to the identification of IODVA1.

a) Brian E. Hall, Dafna Bar-Sagi, **Nicolas Nassar** "The Structural Basis for the transition from RasGTP to RasGDP*" Proc. Natl. Acad. Sci. USA* **99**, 12138-12142 (2002). PMID: 12213964

b) Bradley Ford, Karlheinz Skowronek, Sean Boykevitch, Dafna Bar-Sagi, **Nicolas Nassar** "Structure of the G60A mutant of Ras: Implications for the Dominant Negative Effect" *J. Biol. Chem.* **280**, 25697–25705 (2005). PMID: 15878843

c) Bradley Ford, Viktor Hornak, Holly Kleinman, **Nicolas Nassar** "Structure of a transient intermediate for GTP hydrolysis by Ras" *Structure with Folding and Design* **14**, 427-436 (2006). PMID: 16531227

d) **Nicolas Nassar**, Kavita Singh, and Miguel Garcia-Diaz "Structure of the dominant negative S17N mutant of Ras" *Biochemistry* **49**, 1970-1974 (2010). PMID: 20131908

5. In collaboration with Dr. Nick Carpino (Stony Brook University), I investigated the structure/function of the UBASH3/Sts family of proteins. We showed for the first time that these proteins form a distinct family of protein tyrosine phosphatases (PTPases) structurally and mechanistically distinct from the classical phosphatases exemplified by PTP-1B. Interestingly, and despite strong sequence homology especially for those active side residues, UBASH3B/Sts-1 has a stronger PTPase activity than UBASH3A/Sts-2. We identified a few residues lining the active site responsible for this discrepancy in catalytic activity. We also showed that dually ubiquitinated and phosphorylated proteins are substrates for UBASH3/Sts proteins. We are following up on our findings and studying the role of Sts proteins in leukemia, breast cancer and head and neck cancer.

   a) Anatoly Mikhailik, Bradley Ford, James Keller, Yunting Chen, **Nicolas Nassar**, and Nick Carpino "A phosphatase activity of Sts-1 contributes to the suppression of TCR signaling" *Molecular Cell* **27**, 486-487 (2007). PMID: 17679096

   b) Yunting Chen, Jean Jakoncic, Nick Carpino, **Nicolas Nassar** "Structural and Functional Characterization of the 2H-phosphatase domain of Sts-2 reveals an Acid-Dependent Phosphatase Activity" *Biochemistry* **48**, 1681-1690 (2009). PMID: 19196006

   c) Yunting Chen, Jean Jakoncic, Kathlyn A. Parker, Nick Carpino, **Nicolas Nassar** "Structures of the Phosphorylated and VO_3-bound 2H-Phosphatase Domain of Sts-2" *Biochemistry* **48**, 8129-8135 (2009). PMID: 19627098

   d) Susumu Goyama, Janet Schibler, Anjelika Gasilina, Mahesh Shrestha, Shan Lin, Kevin A. Link, Jianjun Chen, Susan P. Whitman, Clara D. Bloomfield, Deedra Nicolet, Salam Assi, Anetta Ptasinska, Olaf Heidenreich, Constanze Bonifer, **Nicolas N. Nassar**, James C. Mulloy "UBASH3B/Sts-1-CBL axis regulates myeloid proliferation in human preleukemia induced by AML1-ETO" *Leukemia* **30**, 728-739 (2016). PMID: 26449661

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/nicolas.nassar.1/bibliography/40754844/public/?sort=date&direction=descending

For New and Renewal Applications – DO NOT SUBMIT UNLESS REQUESTED
PHS 398 OTHER SUPPORT

There is no "form page" for reporting Other Support. Information on Other Support should be provided in the format shown below.

*Name of Individual: **Nicolas N. Nassar, PhD**
Commons ID: **nnassar**

Other Support – Project/Proposal

***Title**: Functional characterization of the role of distinct domains of ATM and the impact of sequence variants on the DNA damage response

Major Goals: Goals are to establish a system in ATM-deficient human cells, based upon assays related to the cellular response to DSBs, to systematically predict the pathogenicity of individual germline ATM VUS and to elucidate the specific roles in the DSB response of distinct regions throughout ATM, including the effect of mutations in the NBS1-binding domain and 3D structural effects of FATKIN mutations

*Status of Support: Active

Project Number: GM134731

Name of PD/PI: Andreassen

*Source of Support: NIH

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: 08/20/2019-05/31/2023

* Total Award Amount (including Indirect Costs): $1,254,818

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022	.48 calendar

***Title**: Targeted Inhibition in Leukemia

Major Goals: Goals are to study the mechanism of action of the small molecule IODVA1 and to validate VAV3 as the target, to identify the binding site on VAV3 and to validate it, and to test the efficacy of IODVA1 in PDX models of Ph+ and Ph-like acute lymphoblastic leukemia.

*Status of Support: Active

Project Number: R01 CA237016

Name of PD/PI: Nassar

*Source of Support: NIH

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: 07/08/20-06/30/2024

* Total Award Amount (including Indirect Costs): $1,971,197

Name of Individual: Nassar, Nicolas N.
Commons ID: nnassar

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022	3 calendar
2. 2023	3 calendar
3. 2024	3 calendar

***Title**: Pharmacological Inhibition of the Vav3/Rac axis in TKI-resistant PH+ B-ALL - Year 3

Major Goals: To complete pre-clinical and toxicity studies to move IODVA1 into a phase I clinical trial.

*Status of Support: Active

Project Number: n/a

Name of PD/PI: Nassar

*Source of Support: CCHMC – Innovation Fund

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: (MM/YYYY) (if available): 11/01/2020-05/31/22

* Total Award Amount (including Indirect Costs): $100,000

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022	0.6 calendar

***Title**: Delineation of Transcriptomic and Phosphoproteomic Landscapes that Mediate Response to Novel Targeted Therapy in TKI-Refractory B-ALL

Major Goals: To study the effects of the small molecule IODVA1 on the transcriptome and phosphor-proteome of PDX cells.

*Status of Support: Active

Project Number: n/a

Name of PD/PI: Nassar

*Source of Support: CCHMC - CpG

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: (MM/YYYY) (if available): 07/01/21-06/30/22

* Total Award Amount (including Indirect Costs): $100,000

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022	0.12 calendar

Name of Individual: Nassar, Nicolas N.
Commons ID: nnassar

*__Title__: Target Inhibition of Vav3/Rac in Leukemia and other Neoplasia

Major Goals: To validate VAV3 as a target in human cancer.

*Status of Support: Active

Project Number: n/a

Name of PD/PI: Nassar

*Source of Support: Sanofi

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: (MM/YYYY) (if available): 12/01/20-12/31/2022

* Total Award Amount (including Indirect Costs): $125,001

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2022	0.6 calendar

PENDING

*__Title__: Insights into BRCA2 Function: Novel Domain-Specific Activities and Interactions

*__Major Goals__: Proposed research will study the structure/function relationship and contribution of various domains of BRCA2 to homologous recombination and if the various mutants found in disease are of significance.

*Status of Support: pending

Project Number:

Name of PD/PI: Andreassen

*Source of Support: NIH

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: 07/01/22-06/30/27

* Total Award Amount (including Indirect Costs): $2,429,676

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2023	0.9 calendar months
2. 2024	0.9 calendar months
3. 2025	0.9 calendar months
4. 2026	0.9 calendar months
5. 2027	0.9 calendar months

*__Title__: Small molecules targeting Cdc42 for immunotherapy modulation.

Name of Individual: Nassar, Nicolas N.
Commons ID: nnassar

*__Major Goals__: To study how the small molecule CASIN binds to and inhibits the small GTPase CDC42 and how pharmacological inhibition of CDC42 affects the immune system.

*Status of Support: pending

Project Number:

Name of PD/PI: Guo/Zheng

*Source of Support: NIH

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: 05/01/22-04/30/27

* Total Award Amount (including Indirect Costs): $3,261,708

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2023	0.6 calendar months
2. 2024	0.6 calendar months
3. 2025	0.6 calendar months
4. 2026	0.6 calendar months
5. 2027	0.6 calendar months

*__Title__: Novel Inhibitors for the Treatment of Relapsed/Recurrent Leukemia with Activated RAS

*__Major Goals__: Proposed research will validate the VAV3/RAC signaling pathway as a target in RAS-activated leukemia and to test the efficacy of the IODVA1/MAPK-inhibitor combinations in PDX models of R/R pediatric RAS-activated B-ALL and AML.

*Status of Support: pending

Project Number:

Name of PD/PI: N. Nassar

*Source of Support: Elsa U. Pardee

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: 07/01/22-06/30/23

* Total Award Amount (including Indirect Costs): $109,828

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2023	1.2 calendar months

*__Title__: Novel Inhibitors for the Treatment of Relapsed/Recurrent Leukemia with Activated RAS/MAPK

Name of Individual: Nassar, Nicolas N.
Commons ID: nnassar

***Major Goals**: Proposed research will validate the VAV3/RAC signaling pathway as a target in RAS/MAPK-activated leukemia and to test the efficacy of the IODVA1/MAPK-inhibitor combinations in PDX models of R/R pediatric RAS/MAPK-activated B-ALL and AML.

*Status of Support: pending

Project Number:

Name of PD/PI: Nassar

*Source of Support: Leukemia Lymphoma Society

*Primary Place of Performance: Cincinnati Children's Hospital Medical Center

Project/Proposal Start and End Date: 07/01/22-06/30/25

* Total Award Amount (including Indirect Costs): $600,000

* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2023	1.2 calendar months
2. 2024	1.2 calendar months
3. 2025	1.2 calendar months

IN-KIND

*Summary of In-Kind Contribution: N/A

***Overlap** (summarized for each individual): no overlap