מכון ויצמן למדע
WEIZMANN INSTITUTE OF SCIENCE

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Dear Search Committee, June 06, 2022

I am writing to apply for the Assistant Professor position (Job # JPF01546) in the Department of Botany and Plant Sciences at The University of California, Riverside. I am currently a postdoctoral scholar working with Professor Asaph Aharoni in the Department of Plant and Environmental Sciences at the Weizmann Institute of Science, Israel. My research focuses on the biosynthesis of valuable triterpenoids and their roles in plant adaptive responses. This requires the use of cutting edge techniques such as metabolomics, nuclear magnetic resonance and mass spectrometry imaging, which I have mastered during my training at the Weizmann Institute. I am very enthusiastic about contributing to your department.

Isoprenoids are the most diverse group of natural products with countless functions and biotechnological applications. Still their biosynthetic pathways are mostly uncharacterized. One of my research activities has led to the discovery of the entire biosynthetic pathway of triterpenoid saponins. In the resulting paper, published in *Nature Chemical Biology,* I characterized ten new enzymes using metabolomics, NMR and multiple molecular biology techniques. The most profound findings in this project were (a) the hijacking of the Cellulose Synthase-Like (CSL) protein from primary cell wall biosynthesis, by the triterpenoid saponin metabolic pathway, and (b) the discovery of the first fucosyltransferase (FucT), that acts on secondary metabolites. This work resulted in two patents. I received Travel Awards from the Metabolomics Society and the Austrian Drug Screening Institute to present this work at scientific meetings, and I was awarded a prize for outstanding achievements in postdoctoral research.

Further research on the CSL proteins led to finding a missing link in the biosynthesis of antinutritional steroidal glycoalkaloids in tomato. In addition, I have discovered another CSL protein that lacks enzymatic activity and acts as a scaffold, enabling functionality of other biosynthetic enzymes in the pathway. This project involved extensive use of metabolomics and mass spectrometry imaging, and resulted in a manuscript recently submitted to high impact journal.

My research on the first fucosyltransferase paved the way to the discovery of additional FucTs modifying triterpenoid saponins in monocotyledonous plants. For this research, I co-authored a grant with Prof. Aharoni funded by the Mizutani Foundation for Glycoscience. This project is summarized in a manuscript currently at the last stage of preparation. I was also invited as a speaker to share the details of this research during the Metabolomics 2022 meeting in Valencia.

In another project, I studied the convergent evolution of cannabinoid biosynthesis and diversity in non-cannabis plant species. This resulted in a manuscript recently submitted to very high impact journal, and eight patent applications.

My highly collaborative approach has enabled me to study other aspects of plant metabolism. In particular, we have shown how hormonal crosstalk or glycosylation of SAR (Systemic Acquired Resistance) signaling molecules, affect the tradeoff between plant growth and defense (*New Phytologist* and *Molecular Plant*). Additionally, I was part of a research project which provided evidence that, through a process termed 'systemically induced root exudation of metabolites', different microbial communities induce specific systemic changes in tomato root exudation (*PNAS*).

Earlier, during my doctoral studies, under supervision of Professor Swiezewska at the Institute of Biochemistry and Biophysics (PAS), I focused on deciphering the biosynthetic pathway of dolichol, and its involvement in plant development and adaptation to abiotic stresses. This work resulted in 4 first-author publications in *Plant Cell, Plant Physiology, Journal of Lipid Research* and *Biochimica et Biophysica Acta Molecular and Cell Biology of Lipids* and contributed to 2 grants funded by the Polish National Science Centre.

My research goals are to continue to elucidate the evolutionary mechanism underlying structural and functional diversification of triterpenoids. Initially I will focus on three different aspects of this complexity: (i) evolution of

triterpenoid biosynthetic pathways; (ii) diversification of triterpenoids by rare sugars; (iii) deciphering the biosynthetic pathway and function of ecdysone in plants. To achieve these goals, I will use my knowhow in chemistry, biochemistry and molecular biology, and will employ advanced techniques such as metabolomics, proteomics, metabolic imaging, (meta)transcriptomics and (meta)genomics.

In addition to my research, I have worked hard on mastering my mentoring skills. Over the years I worked with many undergraduate and graduate students, and I would be very pleased to actively participate in the department's efforts in boosting the success of its diverse community.

I believe that my expertise and research interests would be a significant addition to the department, and I would welcome potential collaborations with colleagues working in the fields of plant ecology and adaptive responses (plant – insect, plant – microbe and plant – plant interactions), plant evolution, microbial engineering and bioinformatics.

Please find enclosed my curriculum vitae and a list of publications. In addition, you will find my research, teaching and diversity statements that provide further details of the summary above.

I am looking forward to hearing from you.
Sincerely,

Adam Jozwiak

ADAM JOZWIAK, PhD

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EDUCATION

Institute of Biochemistry and Biophysics Polish Academy of Sciences, Warsaw, Poland

October 2008 – September 2013 — **PhD in Biochemistry** (with honors)**,** Department of Lipid Biochemistry (Postgraduate School of Molecular Biology).

University of Warsaw, Warsaw, Poland

October 2004 – June 2008 — **MSc in Chemistry** (with honors), Laboratory of Natural Products Chemistry, Department of Chemistry.

October 2004 – July 2007 — **BSc in Biotechnology**, Laboratory of Plant Biochemistry, Department of Biology.

RESEARCH EXPERIENCE

Weizmann Institute of Science, Rehovot, Israel

April 2019 – present — **Research Assistant, Department of Plant and Environmental Sciences.**

June 2015 – March 2019 — **Postdoctoral Fellow, Department of Plant and Environmental Sciences –** Investigating the biosynthesis and function of triterpenoids in plants.

Institute of Biochemistry and Biophysics Polish Academy of Sciences, Warsaw, Poland

October 2013 – May 2015 — **Postdoctoral Fellow, Department of Lipid Biochemistry –** Investigating the role of polyprenol reductases in *Arabidopsis thaliana*.

October 2008 – September 2013 — **PhD Project, Department of Lipid Biochemistry** – The biosynthesis of dolichols in *A. thaliana* - effect of stress on the subsequent steps of the pathway.

Laboratory of Mass Spectrometry, Institute of Organic Chemistry, PAS, Warsaw, Poland

April 2015 — Project: Structural analysis of pharmaceuticals and their contaminations.
Supervisor: Witold Danikiewicz PhD, Professor

University of Glasgow, Institute of Molecular Cell and Systems Biology, Glasgow, UK

December 2014 — Project: Studies on the effect of abiotic stress on root architecture.
Supervisor: Anna Amtmann PhD, Professor

Tohoku University, Institute of Multidisciplinary Research for Advanced Materials, Sendai, Japan

August 2014 — Project: Isolation and analysis of rubber-like compounds from mangrove plants and herbs.
Supervisor: Hiroshi Sagami PhD, Professor

University Roma Tre, Department of Biology, Rome, Italy

October 2011 — Project: Effect of hypolipidemic drug simvastatin on rat muscle performance.
Supervisor: Valentina Pallottini PhD, Professor

University of Stockholm, Department of Biochemistry and Biophysics, Stockholm, Sweden

October 2009 Project: Coenzyme Q, tocochromanols and their derivatives as gene expression modulators.
Supervisor: Gustav Dallner MD, Professor

Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden

November 2009 Training on HPLC with UV/EC/Radiomatic detectors for analysis of lipids with antioxidant activity.
Supervisor: Kerstin Brismar MD, Professor

RESEARCH GRANTS

2021 – 2022 Principal Investigator: Asaph Aharoni PhD
Weizmann Institute of Science, Israel
Mizutani Foundation for Glycoscience
Role: Co-author. I provided preliminary data, developed the aims, and wrote the grant.

2018 – 2022 Principal Investigator: Asaph Aharoni PhD
Weizmann Institute of Science, Israel
Israel Ministry of Agriculture
Role: Co-author. I provided preliminary data, developed the aims, and wrote the grant with PI.

FELLOWSHIPS AND AWARDS

2022 The Azrieli systems biology innovative award.
2020: Feinberg Graduate School prize for outstanding achievements in postdoctoral research.
2019: Metabolomics Society Early Career Travel Award.
2016: Dean of Faculty Fellowship for postdoctoral fellows, Weizmann Institute.
2014: Royal Society of Edinburgh - Research Fellowship.
Japan Society for the Promotion of Science (JSPS) - Research Fellowship.
2010 and 2012: Intramural grant from the IBB PAS Postgraduate School of Molecular Biology for the best short-term research project.
2009: Mazovian Scholarship granted to most promising PhD students in Mazovia voivodeship for innovative research ideas.

PATENTS

1. WO 2020/049572 A1 – Cellulose-synthase-like Enzymes And Uses Thereof.
2. IL 268269 D0 – Production Of High-value Saponins By The Use Of Cellulose-synthase-like Family Enzymes.
3. Acyl activating enzyme and any transgenic cell, tissue, and organism comprising same, US Patent Application, submitted.
4. Polyketide synthase and any transgenic cell, tissue, and organism comprising same, US Patent Application, submitted.
5. Polyketide cyclase and any transgenic cell, tissue, and organism comprising same, US Patent Application, submitted.
6. Prenyltransferase and any transgenic cell, tissue, and organism comprising same, US Patent Application, submitted.
7. Cannabichromenic acid synthase and any transgenic cell, tissue, and organism comprising same, US Patent Application, submitted.
8. Transgenic helichrysum umbraculigerum cell, tissue, or plant, US Patent Application, submitted.
9. Alcohol acyltransferase and a transgenic cell, tissue, and organism comprising same, US Patent Application, submitted.
10. Uridine diphosphate-glycosyltransferase and a transgenic cell, tissue, and organism comprising same, US Patent Application, submitted.

PUBLICATIONS

Published in peer-reviewed journals

1. Sonawane PD, **Jozwiak A**, Barbole R, Panda S, Abebie B, Kazachkova Y, Gharat SA, Ramot O, Unger T, Wizler G, Meir S, Rogachev I, Doron-Faigenboim A, Petreikov M, Schaffer A, Giri AP, Scherf T, Aharoni A. 2-oxoglutarate-dependent dioxygenases drive expansion of steroidal alkaloid structural diversity in the genus Solanum. *New Phytol.* 2022 Mar 3. doi: 10.1111/nph.18064. Epub ahead of print. PMID: 35238413.
2. Panda S, **Jozwiak A**, Sonawane PD, Szymanski J, Kazachkova Y, Vainer A, Vasuki Kilambi H, Almekias-Siegl E, Dikaya V, Bocobza S, Shohat H, Meir S, Wizler G, Giri AP, Schuurink R, Weiss D, Yasuor H, Kamble A, Aharoni A. Steroidal alkaloids defence metabolism and plant growth are modulated by the joint action of gibberellin and jasmonate signalling. *New Phytol*. 2022 Feb;233(3):1220-1237. doi: 10.1111/nph.17845. Epub 2021 Dec 3.
3. Baczewska-Dąbrowska, A.H., Dmuchowski, W., Gozdowski, D., Gworek, B., **Jozwiak A**, Swiezewska, E., Dabrowski, P., Suwara, I. The importance of prenol lipids in mitigating salt stress in the leaves of *Tilia* × *euchlora* trees. *Trees* (2021). https://doi.org/10.1007/s00468-021-02214-8
4. Cai J, **Jozwiak A**, Holoidovsky L, Meijler M.M, Meir S, Rogachev I, Aharoni A. Glycosylation of N-Hydroxy-Pipecolic Acid Equilibrates between Systemic Acquired Resistance Response and Plant Growth. *Molecular Plant*. (2021) 14(3), DOI:https://doi.org/10.1016/j.molp.2020.12.018
5. **Jozwiak A**, Sonawane PD, Panda S, et al. Plant terpenoid metabolism co-opts a component of the cell wall biosynthesis machinery. *Nat Chem Biol*. (2020);16(7):740-748.
6. Sonawane PD, **Jozwiak A**, Panda S, Aharoni A. 'Hijacking' core metabolism: a new panache for the evolution of steroidal glycoalkaloids structural diversity. *Curr Opin Plant Biol*. (2020); 55:118-128.
7. Dmuchowski W, Baczewska-Dąbrowska A, Gozdowski D, Brągoszewska P, Gworek B, Suwara I, Chojnacki T, **Jozwiak A**, Swiezewska E. 2021. Effect of salt stress in urban conditions on two *Acer* species with different sensitivity. *PeerJ* 9:e10577
8. Dmuchowski, W., Brągoszewska, P., Gozdowski, D. Baczewska-Dabrowska A, Chojnacki T, **Jozwiak A**, Swiezewska E, Suwara E, Gworek B. Strategies of urban trees for mitigating salt stress: a case study of eight plant species. *Trees* (2020). https://doi.org/10.1007/s00468-020-02044-0
9. Korenblum E, Dong Y, Szymanski J, Panda S, **Jozwiak A**, Massalha H, Meir S, Rogachev I, Aharoni A. Rhizosphere Microbiome Mediates Systemic Root Metabolite Exudation by Root-to-Root Signaling. *Proc Natl Acad Sci USA* (2020) 18;117(7):3874-3883.
10. Cárdenas P.D, Sonawane P.D, Heinig U, **Jozwiak A**, et al. Pathways to defense metabolites and evading fruit bitterness in genus Solanum evolved through 2-oxoglutarate-dependent dioxygenases. *Nat Commun* (2019) 10: 5169.
11. Gryz E, Perlińska-Lenart U, Gawarecka K, **Jozwiak A**, et al. Poly-Saturated Dolichols from Filamentous Fungi Modulate Activity of Dolichol-Dependent Glycosyltransferase and Physical Properties of Membranes. *Int J Mol Sci*. (2019); 20(12):3043.
12. **Jozwiak A**, Gutkowska M, Gawarecka K, Surmacz L, Buczkowska A, Lichocka M, Nowakowska J, Swiezewska E. PolyPrenol ReDuctase 2 deficiency is lethal in Arabidopsis due to male sterility. *Plant Cell* (2015) 27: 3336-3353.
13. **Jozwiak A,** Lipko A, Kania M, Danikiewicz W, Surmacz L, Witek A, Wojcik J, Zdanowski K, Paczkowski C, Chojnacki T, Poznanski J, Swiezewska E. Modelling of dolichol mass spectra isotopic envelopes as a tool to monitor isoprenoid biosynthesis. *Plant Physiology* (2017) 174(2): 857-874.
14. Dmuchowski W, Bragoszewska P, Gozdowski D, Baczewska-Dabrowska A, Chojnacki T, **Jozwiak A**, Swiezewska E, Gworek B, Suwara I. Strategy of Ginkgo biloba L. in the mitigation of salt stress in the urban environment. *Urban Forestry & Urban Greening* (2019) 38: 223-231.
15. Milewska-Hendel A, Baczewska A.H, Sala K, Dmuchowski W, Brągoszewska P, Gozdowski D, **Jozwiak A,** Chojnacki T, Swiezewska E, Kurczynska E. Quantitative and qualitative characteristics of cell wall components and prenyl lipids in the leaves of Tilia x euchlora trees growing under salt stress. *PLOS ONE* (2017) 12(2): e0172682.
16. Baczewska A. H, Dmuchowski W, **Jozwiak A**, Gozdowski D, Brągoszewska P, Dąbrowski P, Swiezewska E. Effect of salt stress on prenol lipids in the leaves of Tilia 'Euchlora'. *Dendrobiology* (2014) 72: 177-186.
17. **Jozwiak A**, Brzozowski R, Bujnowski Z, Chojnacki T, Swiezewska E. Application of Supercritical CO_2 for extraction of polyisoprenoid alcohols and their esters from plant tissues. *J. Lipid Res.* (2013) 54: 2023 – 2028.

18. **Jozwiak A**, Ples M, Skorupinska-Tudek K, Kania M, Dydak M, Danikiewicz W, Swiezewska E. Sugar availability modulates polyisoprenoid and phytosterol profiles in *Arabidopsis thaliana* hairy root culture. *Biochimica et Biophysica Acta Molecular and Cell Biology of Lipids* (2013) 1831: 438–447.
19. Segatto M, Manduca A, Lecis C, Rosso P, **Jozwiak A**, Swiezewska E, Morena S, Trezza V, Pallottini V. Simvastatin treatment highlights a new role for the isoprenoid/cholesterol biosynthetic pathway in the modulation of emotional reactivity and cognitive performance in rats. *Neuropsychopharmacology* (2014) 39: 841-854.
20. Trapani L, Segatto M, **Jozwiak A**, Swiezewska E, Pallottini V. HMG CoA reductase inhibition by Simvastatin gets rat β-Myosin Heavy Chain disappeared: a statin paradox. *Open Journal of Molecular and Integrative Physiology*. (2013) 3:1-5.
21. Lefeber DJ, Brouwer AP, Morava E, Riemersma M, Schuurs-Hoeijmakers JH, Absmanner B, Verrijp K, Akker WM, Huijben K, Steenbergen G, Reeuwijk J, **Jozwiak A**, Zucker N, Lorber A, Lammens M, Knopf C, Bokhoven H, Grünewald S, Lehle L, Kapusta L, Mandel H, Wevers RA. Autosomal recessive dilated cardiomyopathy due to DOLK mutations results from abnormal dystroglycan *O*-mannosylation, *PLoS Genet*. (2011) 7: e1002427.
22. Trapani L, Melli L, Segatto M, Trezza V, Campolongo P, **Jozwiak A**, Swiezewska E, Pucillo LP, Moreno S, Fanelli F, Linari M, Pallottini V, Effects of MHC plasticity induced by HMGCoA-reductase inhibition on skeletal muscle functions, *FASEB J.* (2011) 25: 4037-47.
23. Zhang J, Angala SK, Pramanik PK, Li K, Crick DC, Liav A, **Jozwiak A**, Swiezewska E, Jackson M, Chatterjee D. Reconstitution of functional mycobacterial arabinosyltransferase AftC proteoliposome and assessment of decaprenylphosphorylarabinose analogues as arabinofuranosyl donors, *ACS Chem Biol.* (2011) 6: 819-28.
24. Gajjar D, **Jozwiak A**, Swiezewska E, Alapure B, Parmar T, Johar K, Vasavada AR. Quantification of dolichol in the human lens with different types of cataracts, *Mol Vis.* (2009) 15: 1573-9.
25. Czarnocki S, Wojtasiewicz K, **Jozwiak A**, Maurin J, Czarnocki Z, Drabowicz J. Enantioselective synthesis of (+)-trypargine and (+)-crispine E, *Tetrahedron* (2008) 64: 3176.

Submitted manuscripts

26. **Jozwiak A**, Sonawane PD, Panda S, Dong Y, Meir S, Rogachev I, Aharoni A. Cellulose Synthase Like G is indispensable for steroidal glycoalkaloid production in tomato.
27. Berman P*, De Haro L*, **Jozwiak A*,** Sonawane PD*, Panda S, Dong Y, Cveticanin J, Barbole R, Livne R, Arava S, Scherf T, Shimoni E, Kopitman E, Levin-Zaidman S, Meir S, Rogachev O, Aharoni A. Convergent evolution of the cannabinoids biosynthetic pathway (*authors contributed equally to this work).
28. Gharat A, Sonawane PD, **Jozwiak A**, Barbole R, Rogachev I, Meir S, Giri AP, Aharoni A. The GAME36 acyltransferase is a key enzyme in the biosynthesis of ripe tomato fruit-associated glycoalkaloids.

Manuscripts in preparation

29. **Jozwiak A** et al., Discovery of enzymes involved in the biosynthesis of fucosylated steroidal saponins in *Liriope*.
30. **Jozwiak A** et al., Structural diversification of steroidal alkaloids in genus *Solanum* stems from evolution of GAME8 activity.
31. **Jozwiak A** et al., Engineering triterpenoid saponin production and evaluation of their environmental function in plants.
32. **Jozwiak A** et al., Metabolomic profiling provides insights into biosynthesis and spatial distribution of limonoids in genus *Citrus.*

PRESENTATIONS

Selected oral presentation:

- Metabolomics 2022; Deciphering the Complex Chemical Space and Biosynthetic Routes of Steroidal Saponins in Monocotyledonous Plants, June 19-23, 2022, Valencia, Spain.
- Plant MetaboPeople; Biosynthesis of triterpenoids in plants – a surprising case of molecular "hijacking"; April 26-27, 2022, Agamon Hula, Israel
- 5th International Conference on Plant Synthetic Biology, Bioengineering and Biotechnology; Complex Metabolic engineering of plant factories – from scientific curiosity to industrial application, November 15-17, 2021, Virtual; Society for Biological Engineering.
- TERPNET 2019 - The 14th International Meeting on Biosynthesis, Function and Synthetic Biology of Isoprenoids; Elucidation of the Triterpenoid Saponin Biosynthetic Pathway in Spinach Provides Novel Insights to Glycosylation and Acylation Reactions, August 26-30, 2019, Halle Saale, Germany
- 15th Annual Conference of the Metabolomics Society, Metabolomics 2019; From MS peak to unambiguous metabolite identification using the WeizMass spectral library and LC-MS-SPE-NMR system, June 23-27, 2019, The Hague
- Leibniz Institute of Plant Genetics and Crop Plant Research; A Novel Glycosyltransferase Activity of Cellulose Synthase-Like Enzyme Enables Engineering of the Low-Calorie Natural Sweetener from Licorice, September 02, 2019, Gatersleben, Germany
- Second Austrian Summit on Natural Products; Discovery Of Saponin Biosynthetic Pathway In Spinach; January 13 - 15, 2019 Seefeld, Austria

SERVICE

Ad hock reviewer

Metabolites

The Plant Journal

BMC Genomics

Horticulture Research

SCIENTIFIC SOCIETY MEMBERSHIPS

2019 – present	Metabolomics Society
2015 – present	Polish Biochemical Society

"*My job is not to be easy on people. My job is to take these great people we have and to push them and make them even better*." Steve Jobs

From my early years, through observation of my teachers as well as from my experience as a mentor, I learnt that teaching and mentoring attitude should be challenging yet inviting, supportive and respectful. Student–teacher and mentor–mentee relationships should be based on bilateral fulfillment of expectations. I believe that a student's success is a sum of her/his and mentor's efforts. To accomplish this, I will be equally committed to delivering the best quality messages through thoughtful preparation of course content, and its engaging presentation. I will strive to keep the classroom atmosphere very interactive and collaborative and I will foster student confidence and their active participation.

My training as a chemist, biochemist and molecular biologist has provided me with a strong foundation in organic and analytical chemistry, biochemistry and plant natural products, and I am thus prepared to teach all core undergraduate courses in these disciplines. I also envision teaching and developing electives based on my research background and on the needs and wants of the department and students. These could include courses on metabolomics, plant natural product chemistry, proteomics and advanced analytical chemistry. These electives would contain a mix of traditional lecturing and coursework supplemented with a survey of classic and current literature to demonstrate how these concepts are applied in research.

My mentoring experience started when I was a master's student. Since then, I mentored in the lab many undergraduate and graduate students as well as postdoctoral fellows. As we are all unique, the way I mentored had to be adjusted accordingly to each and every student, to ensure the best teaching experience and the student's success. I understood that the less room we keep for insinuations, the better relations we can build with students, and the more involved they become in their studies and research. I also learnt that mutual respect and honesty create a strong bond between mentor and mentee. That is why, I always acknowledge mistakes and failures, and I try to teach my trainees that recognition of mistakes are the best opportunity to learn and improve. My teaching philosophy strongly encourages sharing problems and mistakes and I assure my trainees that they can always come to me, and together we will think through the best possible solution to issue. To foster this collaborative approach, I will keep a friendly and respectful atmosphere in the lab. In the lab we will have well organized weekly meetings, with all the group members discussing the progress of the research and all the problems that we faced. During the meeting, I will encourage everybody to share with the group in an inclusive atmosphere. I am sure that by open discussion we will all learn a lot. In addition to that, I will have weekly personal face to face meetings with each of the group members to discuss their work progress in detail (detailed planning and problem solving) and this will also be an opportunity to keep a more personal and encouraging atmosphere. I will make sure that all members of the lab feel comfortable and that they can always come and ask for help and suggestions.

Scientifically, I will ensure that my mentees have access to all the necessary tools and training that will prepare them for future careers. I will keep my lab very multidisciplinary and I will encourage exchange of knowledge between students to boost their common scientific knowledge, and to increase chances of success. My students will develop aspects of their projects according to their interest. This will foster their internal drive and satisfaction. To encourage the broadening of their research interest I will set up monthly Journal Clubs where we will share the most interesting current research. My students will also be welcome to attend scientific meetings and workshops and will be supported to participate in summer internships. I am sure this complete plan will prepare my lab members for success in their future careers.

Functional Evolution of Triterpenoids

Introduction.

Plants, the finest chemists that have ever existed, produce hundreds of thousands of metabolites with central roles in organismal survival and homeostasis of ecosystems[1]. Diversification of these metabolites relies on evolving multifunctional enzymes. Triterpenoids are among the most ancient and structurally diverse group of natural products, whose complexity originates from a multiplicity of skeletal decorations by processes such as **hydroxylations**, oxidations, **glycosylations**, acylations and more[2]. However, our current knowledge of the nature of the enzymes and their mode of action in generating this diversity has remained incomplete. This diversity of triterpenoids in conjunction with incomplete knowledge of these metabolic pathways has offered me a golden opportunity to research the basics of this key area of metabolism and the respective biotechnological applications.
I will initially focus on the following objectives collectively summarized in the schematic shown in Figure 1. My particular focus will be on distinct aspects of terpenoid biosynthesis summarized in the three projects proposed below.

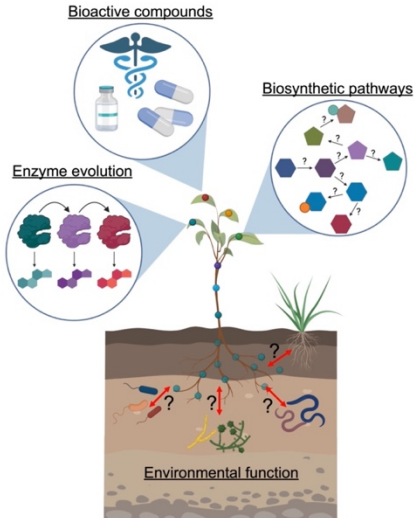

Figure 1. Overview of research proposed in this statement.

Project 1. Ecdysone biosynthesis and function in plants.

Background: Ecdysone, the insect molting hormone, is also present in many plants including my chosen model system quinoa (*Chenopodium quinoa*)[3]. However, thus far ecdysone's biosynthetic pathway and biological function in plants has remained an enigma. To overcome this deficiency, I have generated an EMS population of quinoa mutants and isolated three lines devoid of ecdysone, as examined by the LC-MS analytical platform (Figure 2). Chemical analyses of the precursor molecule (lathosterol) and the end product (ecdysone) suggested involvement of at least 6 enzymatic steps. Based on this assumption, I checked the potential detectable intermediates within the pathway using LC-MS, and obtained evidence for this hypothesis. Furthermore, using grafting experiments between the mutants and the wildtype quinoa, I established that ecdysone is synthesized in shoots and transported to roots, and exuded to the rhizosphere (Figure 3). These 3 findings led to the following questions:

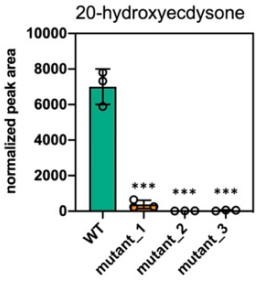

Figure 2 Ecdysone is missing in quinoa mutants.

Aim 1-1. Characterize the ecdysone biosynthetic pathway.

My lab will use several approaches to decipher the biosynthetic pathway using quinoa as the model system. These approaches include: (**i**) Genotyping by sequencing of the mutants. (**ii**) Transcriptomic and proteomic analyses of mutants to find differentially expressed genes and the abundance of their corresponding proteins. (**iii**) Metabolic labeling with precursors of the pathway, and metabolomic analyses of differentially accumulating labeled intermediates in the mutants. (**iv**) Use of a hairy root system (established by me) to test the function of candidate genes, by complementation of the mutant background, and by silencing (RNAi or CRISPR-Cas9) in WT.

Aim 1-2. Distribution and transport mode of ecdysone from shoot to root.

(**i**) Mass Spec Imaging of the quinoa tissues to characterize spatial distribution of ecdysone. (**ii**) Screening the EMS population for ecdysone transporter mutants, using ecdysone presence in the shoot, but not in the root/media. (**iii**) Visualization of transport and exudation of the fluorescent derivative of ecdysone. (**iv**) Define cell-type specific transcriptome, and search for the putative transporter(s). (**v**) Use fluorescent ecdysone derivative to screen the library of transporters in a SmFRET (single molecule FRET) experiment.

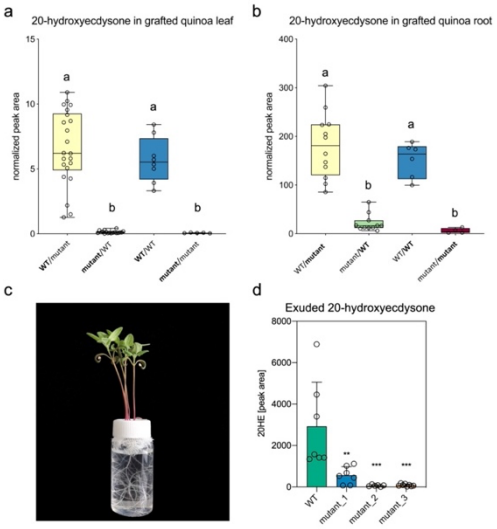

Figure 3. (a, b) 20-hydroxyecdysone content in leaves and roots of quinoa grafted plants. (c, d) Quinoa exudes 20HE to the rhizosphere.

Aim 1-3. Function of ecdysone in plants.

(**i**) Analyze the quinoa microbiome (Wild Type/mutant) with particular focus on bacteria, fungi and nematodes. (**ii**) Assess the interaction between quinoa and root nematodes. (**iii**) Explore the influence of microbiome on ecdysone production/exudation. (**iv**) Study the allelopathy between quinoa and neighboring plants.

Project 2. Diversification of triterpenoids by rare sugars.

Background: Triterpenoid saponins (e.g., QS-21, digitoxin or ophiopogonin B, Figure 4a) are used in modern medicine for treatment of various ailments[4,5,6]. **However, lack of characterized biosynthetic pathways and limited knowledge on enzymes producing 'exotic' sugars (D-fucose, D-quinovose, D-digitoxose and many others), has limited production of these compounds and at high cost** (Figure 4c). Despite our discovery of first triterpenoid modifying fucosyltransferase (Figure 4b; Jozwiak et al., *Nature Chemical Biology* 2020), engineering the production of fucosylated saponins in heterologous systems has remained difficult because of the low availability or lack of certain building blocks (e.g., UDP-α-D-fucose)[2]. I will fill the existing knowledge gap by fulfilling the following research aims:

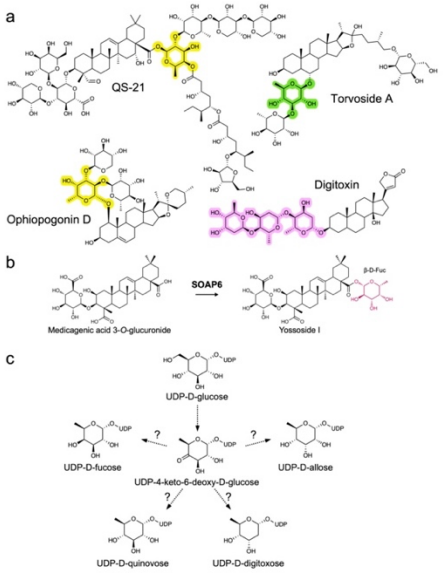

Figure 4. (a) Representative structures of triterpenoids modified with exotic sugars. (b) Enzymatic reaction catalyzed by SOAP6, first characterized fucosyltransferase in plants. (c) Scheme depicting still undisclosed biosynthetic routes of exotic sugars.

Aim 2-1. Characterize the enzymes for biosynthesis of exotic sugars.

(**i**) Metabolomic and transcriptomic profiling of plants producing saponins with exotic sugars. (**ii**) Bioinformatic analyses and selection of candidate genes. (**iii**) *in vitro* and *in vivo* functional characterization of the encoded putative enzymes by metabolite analyses (HILIC or ion chromatography). (**iv**) Structural studies of the resulting compounds by NMR.

Aim 2-2. Triterpenoid related glycosyltransferases (GTs) utilizing rare sugars.

To discover new GTs that decorate triterpenoids with rare sugars, my lab will: (**i**) perform metabolic profiling and transcriptomic analyses of plants producing saponins with rare sugars. (**ii**) Select and functionally validate putative GTs. (**iii**) Find structural protein motifs responsible for specificity towards 'exotic' sugars.

Aim 2-3. Engineering production of valuable triterpenoids with rare sugars.

This aim will be fulfilled in heterologous hosts such as tobacco, BY-2 and yeast cells by:
(**i**) Introduction of the rare sugar biosynthetic pathway (implementation of the knowledge gathered in Aim 2-1). (**ii**) Utilization of 'exotic' sugar specific GTs (from Aim 2-2). (**iii**) Metabolic profiling of transgenic organisms, isolation and structural characterization of metabolites.

Project 3. Evolution of triterpenoid biosynthetic pathways.

Background: Cellulose Synthase-Like G proteins (CslG) play crucial roles in biosynthesis of triterpenoids[2,7]. In my research published in *Nature Chemical Biology* I describe unexpected glucuronosyltransferase activity of the ER-localized SOAP5 (CslG) acting on triterpenoids from spinach (Figure 5a, b). In another paper submitted to *Nature Plants* I report that a member of CslG from tomato (GAME15) is a component of cell wall machinery hijacked to act as a scaffold, thereby enabling activity of steroidal glycoalkaloid biosynthetic enzymes (Figure 5c-e). Based on these documented findings of CslG proteins, my lab will continue studying the underlying mechanisms involved in emergence of new enzymatic functions of CsIG responsible for diversification of triterpenoids.

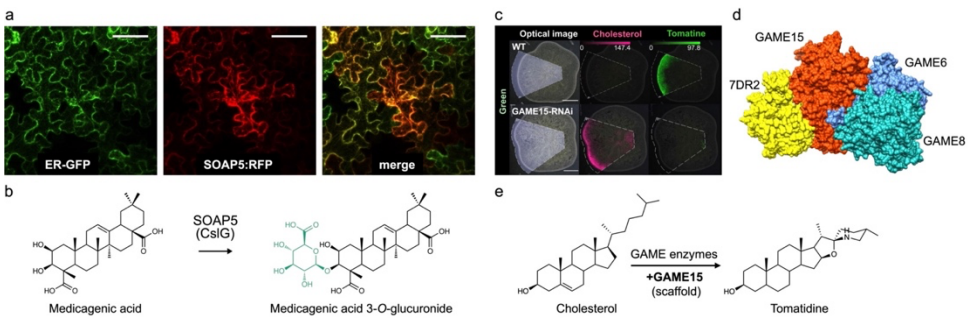

Figure 5. (a) SOAP5 from spinach localizes to the ER. (b) SOAP5 catalyzes attachment of glucuronic acid to the triterpenoid aglycone. (c) Mass spectrometry imaging analysis unravels high accumulation of cholesterol and lack of tomatine in GAME15-RNAi tomato fruit. (d) 3D model representing GAME15 interacting with 7DR2, GAME6 and GAME8. (e) GAME15 is a scaffold protein facilitating production of glycoalkaloids in tomato.

Aim 3-1. How Cellulose Synthase-Like G proteins are redirected to the ER?

(**i**) Bioinformatics of CslGs and closely related CSLs with different subcellular localization (ER, Golgi, plasma membrane). (**ii**) Identification of structural motifs that retain CslG in the ER. (**iii**) Validation by directed mutagenesis and assessment of subcellular localization of modified CSL proteins.

Aim 3-2. Structural characterization of CslG proteins - features responsible for enzymatic or scaffold function.

(**i**) Bioinformatic analyses of catalytically active and inactive CslGs (spinach *vs.* tomato) – analysis of 3D structures using AlphaFold and detection of the active site(s). Modeling of protein-protein contact sites and confirmation by mutagenesis. (**ii**) Identification of the amino acid residues responsible for sugar donor specificity (UDP-Glc vs. UDP-GlcA) and triterpenoid acceptor selectivity (e.g., medicagenic acid). (**iii**) Functional modification studies by directed mutagenesis and assessment of new functionality (*in vitro* reaction and metabolite profiling).

Aim 3-3. Define new functions of other representatives from the CslG family.

(**i**) Large-scale phylogenetic analyses of CSLs from all available plant genomes and transcriptomes for identification of additional CSLs with new functionalities (new substrate specificity, scaffolding role in other pathways, others). (**ii**) Subcellular localization of selected proteins. (**iii**) Functional characterization by silencing in a native plant and overexpression in heterologous systems followed by metabolomic analyses for differential metabolites. (**iv**) Functional evaluation by testing their substrate specificity (*in vivo* and *in vitro*) and possible interactions with other enzymes from the pathway (split ubiquitin, spit luciferase, Co-IP-MS/MS, FLIM-FRET).

Perspectives.

Extensive evolution of scaffolding proteins and biosynthetic enzymes has led to a notable diversity of plant triterpenoids. Plants use this chemo-complexity to communicate with an ever-changing environment. My multi-threaded approach will pave the way to decipher uncharacterized biosynthetic pathways of ecdysteroids and triterpenoid saponins in plants. The proposed projects will result in identification of new biosynthetic enzymes involved in production of exotic sugars in plants and novel glycosyltransferases utilizing these rare carbohydrates to decorate triterpenoids. Research on the evolution of Cellulose Synthase-Like proteins will provide information on mechanisms behind altered subcellular localization and function of these proteins. For example, the outcome of my proposed research will enable us to explain why and how localization to the ER was crucial in gaining new functions, and which structural features are responsible for changes in substrate specificity. Collectively, the gained knowledge will enable metabolic engineering of the entire triterpenoid biosynthetic pathways and extensive analyses of their functions within the environmental context. Furthermore, advanced synthetic biology and microbial fermentation of triterpenoids will lead to understanding of their bioactivity and large-scale production of high-value products independent of cultivation or harvest in nature. In summary, this work will provide a springboard for unlocking an uncharted chemical space of potent triterpenoids with highly valuable biotechnological applications. Output of my research will be highly innovative and of broad interest, especially among biotech companies, hence I will collaborate with **patent** attorneys to protect intellectual property.

My lab will take advantage of existing core units on the UCR campus (metabolomics, proteomics, NMR and microscopy). Additionally, I will energetically pursue establishment of a mass spectrometry imaging facility and metabolite purification laboratory, equipped with state-of-the-art instrumentation. Both will be accessible to the UCR community.

Funding.

I am cognizant of the competitiveness of obtaining funding from the granting agencies in the US. As such, I have planned various experimental and research proposals suitable for different agencies. Project 1 - related to studies on quinoa is deemed suitable for USDA. I will seek funding of health-related Project 2 at NIH. I will propose the 3rd project to NSF. I am also aware that as a new investigator I can simultaneously submit a given proposal to all the three agencies, and I am going to take advantage of this possibility. Furthermore, I will approach not only federal granting agencies but also private sources, such as the Gates Foundation for the quinoa project. During my postdoc I have built a strong network of collaborations with researchers in Israel and in Germany and I will use this opportunity to apply for support from Human Frontier and BARD funds.

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Universal Declaration of Human Rights states in article 2: "Everyone is entitled to all the rights and freedoms set forth in this Declaration, without distinction of any kind, such as race, colour, sex, language, religion, political or other opinion, national or social origin, property, birth or other status." I fully agree with this statement and as a researcher and teacher I will do my best to ensure diversity and inclusion of all the students and personnel on UCR campus.

As a Polish citizen born under communist rule, a first generation college student and a gay man, I understand very well the importance of diversity and inclusion.
From my early years I received a lot of support and encouragement from my parents who were aware that my education was the only way to improve the quality of my life, and that this would affect the entire surroundings and everyone I meet on the way. Despite lack of financial capabilities, they would constantly expose me to new learning possibilities. They would always challenge me in a caring way to become better in whatever I was doing. Later on, during my studies I received a lot of support from my teachers and supervisors that believed it is worth investing in me.
Additionally, being a gay person in a post-communist country was not an easy part of my life. Luckily the feeling of rejection from society was completely absent among my friends, teachers and supervisors.

During my postdoc abroad (many years in Israel) I have been exposed to diversity at its best. I had the chance to build beautiful, friendly relations not only with local Jews and Muslims but also with students from China, India, Brazil, Ethiopia and many more. Altogether, I find the multinational and multicultural atmosphere in the lab very stimulating and enriching. I am sure that the power of human kind comes from its diversity, something we should constantly fight and care for. I know that despite differences we can always find a common language and build a community of equity and inclusion, where we all can thrive and learn from each other.

The path that I have walked from my childhood to graduation with honors from the best University in Poland, to finalizing my doctoral studies and succeeding in my postdoctoral research at one of the best scientific institutes in the World, would not have been possible without help and the feeling of equity and inclusion that I experienced from my family, friends and mentors.

During all these years I gained a lot of experience and understanding of what students or colleagues of different sexualities and from various socio-economic backgrounds may feel. That is why I feel strongly that I will be able to contribute to the preservation of diversity, and to building an environment of inclusion and equity, through teaching in courses and face-to-face mentoring in the lab. Most of the help I received over the years came from amazing and powerful women, now I will give the support back to women by encouraging and helping them with, e.g., scholarship applications for women in STEM (Virginia Heinlein Memorial Scholarship, America's Dream Award, Libbie H. Hyman Memorial Scholarship and many other). Additionally, I will actively support the Office of Diversity, Equity and Inclusion at UCR and the DEI committee at BPS.

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Letter of reference

concerning application for the Assistant Professor position (Job # JPF01546) in the Department of Botany and Plant Sciences at The University of California, Riverside: ADAM JOZWIAK, Ph.D.

June 8, 2022

To Whom It May Concern:

This letter is to convey my strong support of the application of Dr. Adam Jozwiak for the Assistant Professor position (Job # JPF01546) in the Department of Botany and Plant Sciences at The University of California, Riverside.

My name is Ewa Kula-Swiezewska, Ph.D., and I am a professor and a Head of the Laboratory of Lipid Biochemistry at the Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, Poland. I received my Ph.D. in 1990, and professorship - in 2003. I have reviewed over 300 manuscripts in many international journals and numerous grant applications in Poland and internationally. Since 1987, I have published over 150 papers in international journals.

I have known Dr. Adam Jozwiak since 2007 when he did the student internships in our Laboratory. After receiving his M.Sc. diploma he successfully passed (among top 3 candidates) the demanding entrance exams and implemented his doctoral project (2008 – 2013, PhD degree with distinction). Further, he was employed in my group as a postdoctoral fellow until 2015. As a supervisor of his thesis I was impressed by his performance - he designed and implemented the experiments, established several molecular biology methods not used by our team by that time, and finally wrote the relevant manuscripts. Due to his efforts four publications directly linked to the doctoral project have been published, including a paper published in the prestigious journal *The Plant Cell*. Besides the main line of research Dr. Jozwiak was also involved in several side projects, which resulted in twelve additional papers (2009-2022). During his doctoral studies he performed several internships and was a recipient of three external and one intramural research grants.

Since 2015 Dr. Jozwiak worked as a Postdoctoral Fellow and Research Assistant at the Department of Plant and Environmental Sciences, Weizmann Institute of Science, Rehovot, Israel. I am familiar with his achievements through his publications. His findings in the field have greatly advanced our view of biosynthetic mechanisms and cellular role of plant secondary metabolites, and terpenoids in particular. During his time at Weizmann Institute Dr. Jozwiak has published eight publications in highly recognized journals, including *Nat Chem Biol, Nat Commun, Molecular Plant, PNAS*. To achieve this, he established and adopted numerous techniques, such as molecular biology tools, metabolomics, methods of structural analysis of natural compounds (nuclear magnetic resonance and mass spectrometry), plant physiology and biochemical methods.

I cannot emphasize enough that Dr. Jozwiak's work is on the forefront of secondary metabolite biology and bioscience research.
In a nutshell, Dr. Jozwiak's extraordinary work is a clear indication of his eligibility as a candidate for the Assistant Professor position because of the strength and importance of his research. I am positive that his noteworthy research capabilities will enable him to maintain his work generating highly important and influential research and to establish a successful research team at the Department of Botany and Plant Sciences at The University of California, Riverside.

Thank you for your kind consideration of this letter. Please let me know if there is anything further that I can do to provide you with assistance in this process.

Yours faithfully,

Ewa Swiezewska, PhD
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28th June, 2022

Dr. Adam Jozwiak

Tenure position in UCR

Dear Committee Members,

It is my immense pleasure to recommend Dr. Adam Jozwiak for a tenure track position at the Department of Botany and Plant Sciences at The University of California, Riverside. With no doubt Adam has a stellar career trajectory as an independent researcher in any place he will select to join. My recommendation here is based on nearly 7 years of close, day to day interaction with him. My appreciation of Adam as a scientists and as a person is immense and I am not sure that I will ever get the opportunity to recruit many others in his caliber and personality to my team. **He is just extraordinary!.**

Adam's research achievements to date culminated in several major breakthroughs in the field of plant secondary/specialized metabolism. We are now working on several papers with additional exciting and impactful findings which in my view will open new avenues and affect significantly our field of research. I will elaborate the major reasons for this through my letter. Adam's paper in *Nature Chemical Biology* represents a unique amalgamation of molecular biology, biochemistry, synthetic chemistry, analytical chemistry (mass spectrometry, gas and liquid chromatography and NMR) and metabolic engineering of plants and microbial systems. In contrast to other cases from my lab in which the combination of such distant disciplines required many contributors and extensive collaborations, Adam was the major player and hands-on behind all experiments reported. He is extraordinary in experiment planning and most efficiently executes complex experiments requiring diverse expertise. I rank Adam among the first in excellence among dozens or probably more than a hundred members that worked in my group since starting my lab in WIS. He is unquestionably par to the best of the best I have mentored including Samuel Bocobza, currently a Pi at the Volcani center and Prashant Sonawane that has a group leader position at the Max Planck Institute for Chemical Ecology in Jena. As Prashant, Adam was recently awarded our graduate school FGS prize for outstanding achievements in postdoctoral research. Apart from his personal characters I have mentioned above, Adam is very smart, super dedicated and hard worker spending endless time in the lab as well as one of the most multi-tasking individual I have met.

Glycosylation of biomolecules is a widespread phenomenon with great significance to eukaryotes, archaea, bacteria, and viruses. It involves the transfer of one or more sugars of different kinds to an assortment of acceptors

including proteins, oligosaccharides, lipids, and a wide range of small molecules. Glycosylation of small molecules such as plant specialized metabolites has a profound impact since it can greatly modify their solubility, stability, toxicity, storage as well as intra- and intercellular transport. The enormous array of 200,000 and likely more specialized metabolites produced by plants very often exist in plentiful glycoforms, regioselectively glycosylated at different positions and carrying single or multiple sugars. The patterns of glycosylation will also affect the action of plant metabolites in the human body. **In his work, Adam had several core discoveries**. Adam's initial discovery was the outcome of a combined transcriptomics and gene co-expression approach that enabled him to identify for the first time a complete triterpenoids saponins pathway comprising a set of 10 genes and enzymes. One of his major finding was that proteins of the cellulose synthase complex constructing the plant cell wall were 'hijacked' and neofunctionalized to modify and generate structurally different defensive plant specialized metabolites. **Members of this large family of plant proteins were never associated with specialized metabolism.** Adam found that not as expected, a CSL G family member (CSLG) enzyme rather than a UGT family member, transfers glucoronic acid to the C-3 position of a triterpenoid saponin aglycone. To date, the function of merely several CSL proteins was uncovered, however, all of them function in cell wall polysaccharides formation. Adam went further showing the conservation of CSLGs action in triterpenoids glucuronidation among many species and several plant orders.

Adam uncovered several long sought and in some cases the last committed reactions in the biosynthesis of triterpenoid saponins including extensively studied pathways in alfalfa, soy, saponaria, licorice and quinoa. Some of these high-value glucuronidated saponins are exploited at present in the food, cosmetics and pharmaceutical industries. Thus, his findings pave the way for metabolic engineering and production of high-value saponins through microbial fermentation and plant systems. In one case, Adam elucidated the last unknown reaction in the biosynthesis of glycyrrhizin; a triterpenoid saponin produced in licorice decorated with two glucuronic acid moieties at the C-3 position. This pathway is now set for engineering and large-scale commercial production of low-calorie sweeteners with no glycemic index that are several hundred times sweeter than sucrose. It will also likely trigger the discovery of additional CSL enzymes functioning in modification of other classes of terpenoids and specialized metabolites and consequently boost the use of saponins in a range of industrial and agriculture applications.

Further, in his research, Adam identified for the first time a small molecule fucosyl-transferase in plants as fucosylation to date was merely associated with plant protein glycosylation. Interestingly, fucosylation of small molecules requires UDP-D-fucose rather than UDP-L-fucose, the latter serves as a universal sugar donor in all protein glycosylation reactions known at present in any organism. Adam is now in the course of resolving the crystal structure of the newly identified fucosyl transferase enzyme and the results of these experiments will likely shed light on the structural features and evolution of both protein and small molecule fucosylation. Moreover, in the same study, Adam identified the only acyltransferase acetylating a triterpenoid saponin. Together with CSLG and fucosyltransferases, the discovery of these three enzymes has a significant contribution to the understanding

of how some of the most structurally complex saponins are made; e.g. the renowned and commercial QS-21 adjuvant from *Saponaria* species.

The above description covers only a small fraction of the entire set of Adam's research. His research achievements, already at this stage, are truly outstanding and he will no doubt have a distinguished record when he departs my lab. In the past year Adam resolved two major questions we have been working on for a long period of time. Nearly 10 years ago we discovered a metabolic gene cluster in tomato and potato involved in glycolalkaloid metabolism. One gene in this cluster putatively encoding a CSLG could be clearly associated with a role in glycoalkaloids production in tomato; however, till a few months ago we did not know its function. The tomato CSLG is related to the other proteins characterized by Adam earlier from other plant species in which it acts as a triterpenoid glucuronosyltransferase (noted above). Now Adam discovered that the *Solanaceae* CSLG, including in tomato, does not act as an enzyme but rather as a scaffold protein which tethers glycoalkaloid metabolism proteins in a form of a metabolon to the ER membrane. These finding revealed a very interesting protein evolution process in which the core cellulose biosynthesis enzyme (i.e. CesA) evolved in different plant families to either catalyze glycosylation of specialized metabolites while on the other, forming a complex for efficient production of metabolic products. Evolving to either an enzyme of specialized metabolism or a scaffold protein required re-targeting the protein tot the ER rather than to the classical CesA location in the plasma membrane. **Following Adam's discovery we can now engineer and reconstitute the entire glycoalkaloid pathway in plants, experiments which we have been trying with no sucess for nearly a decade by now.** In a related work, Adam identified a cytochrome P450 enzyme (GAME8) as the major factor that determines glycoalkaloid structural diversity in a given *solanaceae* species, whether a tomato or an eggplant (the spiny solanum clade) type alkaloid structure will be formed.

Apart from the impressive set of Adam's achievements I would like to highlight his amazing character. Adam guided and assisted many lab members in different aspects of our work, both in chemistry and biology. He is the most 'loved' person in the lab up to date and everybody wants to work with him. Moreover, he does everything in a calm manner and great modesty. You will immensely enjoy his presence in your department staff and students. It will take my lab a long time to recover once Adam's leaves the lab for a new position as an independent researcher.

Following the above, I cannot think of a better candidate for the tenure track position in your department.

Sincerely yours,

Asaph

Search Committee
Department of Botany and Plant Sciences
University of California, Riverside
2142 Batchelor Hall
University Ave, Riverside, CA 92506

Dear Search Committee,
It is my pleasure to recommend Dr. Adam Jozwiak for the position of Assistant Professor in your department (Job # JPF01546).
I have known Dr. Adam Jozwiak since 2015 when he joined the lab of professor Aharoni as a postdoc. Dr. Jozwiak is the key person in many projects that focused on biosynthesis of triterpenoids in spinach, tomato and other plants with unknown biosynthetic pathways.
Dr. Jozwiak, an outstanding postdoctoral researcher, orchestrated an impressive line of experimental approaches that resulted in the structural characterization of the saponins and glycoalkaloids present in various plants and in the elucidation of their biosynthetic pathways. To achieve this, he applied multiple molecular biology and metabolic analysis tools including mastered by him transcriptomic analysis, metabolomics, mass spec imaging and NMR based structure elucidation. His work resulted in many surprising findings: (A) the identification of a new class of enzymes that have a glucosyltransferase enzymatic activity in saponin biosynthesis, previously annotated as cellulose synthases (and thus elusive of their crucial role in completing the biosynthetic puzzle that the scientific community struggled to solve); (B) discovery of tomato cellulose synthase-like protein acting as a scaffold in the biosynthesis of antinutritional steroidal glycoalkaloids; (C) finding first fucosyltransferases acting on triterpenoids. With this work, Dr. Jozwiak provided the scientific community with essential, missing links in the chain of saponin biosynthesis. Adam's work provides evidence for the evolutionary hypothesis for the emergence of abundance of bioactive molecules in plants via neofunctionalization of existing genes in the plant genomes. From a more applied perspective, with this finding it is now possible to engineer the entire biosynthetic pathways in heterologous systems to facilitate both basic research questions to be pursued and the exploitation of the production of high-value products (as saponins are) in diverse industries and agriculture. Not surprisingly, Dr. Jozwiak's work was disseminated with publications of very high impact.

Through our collaboration, I had the opportunity to work closely with Adam. I was impressed by the immense work of excellent quality that he has achieved. I also had the chance to hold extensive discussions with Dr. Jozwiak. It was clear that he has a sound grasp of both the practical details of his work and of the theoretical background to science. He is a highly motivated researcher, interested in broadening his work in plant specialized metabolism to cover subjects on cell biology, synthetic biology, metabolomics and evolution of metabolism in plant adaptive responses. Equally important, Adam's communication skills were a pleasant experience for me, both his scientific writing and the presentation of his findings to various audiences are highly competent. He is always helpful and supportive, which to my point-of-view, is an essential trait for a scientist as regards both his own advancement and his contribution to the scientific community. Dr. Jozwiak is always keen on enriching his work through new collaborations and acquiring training to keep up to date with the new techniques and research topics.

Taking into account the above, I believe that Dr. Jozwiak is a scientist of the highest caliber and has already shown his potential to greatly contribute to science, along the lines of his definite research vision. I have no hesitation in giving Dr. Jozwiak my highest recommendation for the position of Assistant Professor as a very talented scientist with great potential and undoubted future success. He would be a good catch for any department and I urge you to consider his candidacy seriously.

Yours faithfully,
Ilana Rogachev, PhD
Staff Scientist, responsible for chemical analysis in Asaph Aharoni Lab,
Dept. of Plant and Environmental Sciences,
The Weizmann Institute of Science, Rehovot, Israel.