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: ZOLTAN SZEKELY

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

POSITION TITLE: Research Scientist

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
University of Debrecen, Hungary	MS	05/1992	Chemistry
University of Szeged, Hungary	PhD	05/1997	Bio-organic and Peptide Chemistry
International Centre for Genetic Engineering and Biotechnology (United Nations) Trieste, Italy	Postdoctoral	09/1998	Chemical Biology
National Cancer Institute, Frederick, MD	Postdoctoral	12/2004	Chemical Biology

A. Personal Statement

I am a Chemist and Chemical Biologist with experience in research on various topics of drug design, discovery and delivery. My interdisciplinary background includes a broad spectrum of technologies including computer-aided drug design, classic and automated chemical synthesis and analysis. My knowledge and experience in collaborating with biomedical scientists has proven to be advantageous in achieving complex research goals. I have utilized my unique skill set to investigate a variety of targets in biomedical research including: HIV entry inhibition, retroviral enzyme inhibition (HIV protease and reverse transcriptase as well as HCV protease), the glycobiology of interstitial cystitis, mechanism of action of vancomycin antibiotics, cancer drug conjugates and sequence selective DNA alkylating agents. The past 12 years, I have setup three automated synthesis facilities at the National Cancer Institute, Sequoia Pharmaceuticals Inc., and at the School of Pharmacy at Rutgers, The State University of New Jersey. By setting up the Chemical Biology Core Facility at Rutgers, I provide a unique automated capability to synthesize and analyze chemical compounds and bio-conjugates in a high-throughput format. Since June 2016, I am working as a Co-investigator at the Rutgers Cancer Institute of New Jersey on an antibody-drug conjugate project funded by the Breast Cancer Research Foundation. I am also responsible for planning and executing the chemical synthesis, characterization, analytical and bioanalytical development for research projects on drug delivery systems (nanoparticles, microspheres) for wound healing and the treatment of AIDS as well as lung cancer performed at the School of Pharmacy at Rutgers. While working at Sequoia Pharmaceuticals, I optimized the fragments of an HIV-1 protease inhibitor lead structure and participated in HCV protease inhibitor development. In 2021, I joined the Laboratory of Molecular Design and Synthesis at Rutgers as an analytical chemist. Besides supporting the team's various projects in drug discovery and development, I continue my preclinical research on antibody-drug conjugates as well.

B. Positions, Scientific Appointments, and Honors

2005-08 Staff Scientist, Sequoia Pharmaceuticals, Inc. Gaithersburg, MD.
2009-10 Consultant, Department of Pharmaceutics, Rutgers University, Piscataway, NJ.
2010-20 Research Professor, Department of Pharmaceutics, Rutgers University, Piscataway, NJ.

2020-21 Research Scientist, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ.
2021- Research Scientist, Molecular Design and Synthesis Laboratory, Rutgers University, Piscataway, NJ.

C. Contributions to Science

1. Design, Synthesis and Evaluation of an Antibody-drug Conjugate (ADC). In collaboration with Prof. Joseph R. Bertino, at the Rutgers Cancer Institute of New Jersey, we developed a novel ADC targeting activated matriptase. This unique cancer antigen is expressed on several hard-to-treat tumors including triple negative breast cancer, castrate resistant prostate cancer, non-small cell lung cancer and mantle cell lymphoma. We have shown significant tumor regression in animal models as well as found promising anti-tumor effect while using the ADC in combination with chemotherapeutic agents.

a. Rather, G.M., S.Y. Lin, H. Lin, W. Banach-Petrosky, K.M. Hirshfield, C.Y. Lin, M.D. Johnson, Z. Szekely, J.R. Bertino, *Activated matriptase as a target to treat breast cancer with a drug conjugate.* Oncotarget. 2018. **9**: p. 25983-25992. (PMID: 29899836).

b. Rather, G.M., S.Y. Lin, H. Lin, Z. Szekely, J.R. Bertino, *A Novel Antibody-Toxin Conjugate to Treat Mantle Cell Lymphoma.* Front. Oncol. 2019. 9:258. doi: 10.3389/fonc.2019.00258. (PMID: 31024856).

2. Development of Peptide-based Inhibitors for E2F Transcription Factors. My second collaboration with Prof. Bertino demonstrates a synthetic approach to optimize an anti-tumor peptide. E2F1-3a overexpression (due to amplification or to mutation or loss of the retinoblastoma gene), leads to abnormal cellular proliferation, tumor growth, and invasion. Inhibiting the overexpression of an activating E2F (or multiple E2Fs) is a validated target for the development of novel cancer therapeutics. We synthesized inverso- and retro-inverso analogues of the lead peptide that resulted higher anti-tumor activities both *in vitro* and *in vivo*.

a. Shaik, T., G.M. Rather, N. Bansal, T. Minko, O. Garbuzenko, Z. Szekely, E.E. Abali, D. Banerjee, J.E. Kerrigan, K.W. Scotto, J.R. Bertino. Modeling and antitumor studies of a modified L-penetratin peptide targeting E2F in lung cancer and prostate cancer. Oncotarget. 2018. 9: p. 33249-33257. (PMID: 30279956).

3. Structure Determination and Solid-phase Synthesis of an Antiproliferative Factor from Interstitial Cystitis Patients. Interstitial cystitis a chronic painful urinary bladder disorder characterized by thinning or ulceration of the bladder epithelial lining and effecting about 1 million people in the US alone. I was involved the purification, structure determination of an antiproliferative factor derived from patients diagnosed with interstitial cystitis. After the purification and mass spectrometry based structural studies, I was able to synthesize a sialoglycopeptide using solid-phase peptide synthesis and enzymatic sialization. The following paper and granted patent represent the importance of this project:

a. Keay, S.K., Z. Szekely, T. Conrads, T. Veenstra, J.J. Barchi, C.O. Zhang, K. Koch, K., C.J. Michejda, C. *An antiproliferative factor from interstitial cystitis patients is a novel frizzled 8 protein-related sialoglycopeptide*. Proceedings of The National Academy of Sciences, 2004. **101**: p. 11803-11808. (PMID: 15282374).

b. Keay, S.K., Z. Szekely, T. Conrads, C.J. Michejda, *Antiproliferative Factor and Methods of Use,* Issued US Patent 9,085,604

4. Molecular Modeling of the First Step of the HIV-1 Entry Process to $CD4^+$ Cells. As a part of my doctoral thesis, I have been extensively studying the structure of the CD4 receptor, to design HIV-1 entry inhibitors by using molecular mechanics and dynamics. By starting with the X-ray structure of various domains and carbohydrate conformational investigations by NMR, I was able to establish a structural model for the full (glycosylated) extracellular domain of the CD4 receptor. This model could explain the changes in biological activities of CD4 point mutants, as well as establishing QSAR among small molecule and peptide ligands, before x-ray diffraction data on HIV-1 envelope glycoprotein complexes became available.

a. Szekely, Z., A. Perczel, B. Penke, J. Molnár, *A new method for the interpretation of dynamics trajectories in the conformational analysis of HIV receptor mutants.* Journal of Molecular Structure (Theochem), 1993. **286**: p. 165-182.

b. Szekely, Z., *A new approach for an HIV docking-inhibitor drug designed on the basis of the dual recognition/binding hypothesis between the CD4 receptor and the envelope glycoprotein of the HIV*. Journal of Molecular Structure (Theochem), 1995. **334**: p. 93-100.

c. Szekely, Z., Z. Kónya, A. Becskei, W.P.D. Goldring, A. Perczel, B. Penke, J. Molnár, C.J. Michejda, A. Aszalós, I.G. Csizmadia, *Suggested binding mechanism of the HIV-gp120 glycoproteine to its CD4 receptor,* Journal of Molecular Structure (Theochem), 1996. **367**: p. 159-186.

d. Szekely, Z., L. Torday, C.J. Michejda, A. Aszalós, *Binding between the CD4 receptor and polysulfonated azo-dyes. An exploratory theoretical study on action-mechanism,* Journal of Molecular Structure (Theochem), 1998. **423**: p. 153-159.

5. Sequence Selective DNA Alkylating Agents. At The National Cancer Institute, I hypothesized that sequence selective DNA minor groove binding pyrrole-imidazole polyamides with embedded cyclopropylbenzindole alkylating subunits should have to improved selectivity in cytotoxic effect. An in-depth modeling and synthetic investigation resulted in a Patent filing. The key structural feature of this invention was found in yatakemycin, a natural product that was published 6 months after the patent priority date.

a. Szekely, Z., H.K. Hariprakasha, M.W. Cholody, C.J. Michejda, *DNA-binding Polyamide Drug Conjugates,* PCT/US03/06006. 2002.