

P. Alexander Rolfe

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Experience

EMD Serono Inc. Sr. Director/Director of Bioinformatics (September 2021 - Present / March 2014 - August 2021) Led Bioinformatics group supporting Immunology and Immunology-Oncology at all pipeline stages. Led/supervised predictive biomarker research for Avelumab, Bintrafusp Alfa, Atacicept, Evobrutinib, Enpatoran. Provided and managed bioinformatics support for a major target discovery effort for Lupus. Discovery and development project support for target identification, model selection, and biomarker identification. Led "Bedside to Bench" R&D strategic initiative. Developed practices and community around new 'omics + data science platform. Led applications of machine learning across portfolio - text mining, classification, neural nets. Supervised adoption of single-cell RNASeq processing, analysis, and visualization.

EMD Serono Inc. Associate Director of Bioinformatics (December 2013 - March 2014) Specialized in next-generation sequencing. Designed and implemented company's first cloud-based system for scientific computation using AWS. Supervised and supported development of custom sequencing protocols for antibody library development.

Pathogenica, Inc. VP of Bioinformatics (May 2011 - October 2013) Responsible for design and implementation of Pathogenica's computational infrastructure including capture probe design, sequencing data analysis pipelines for internal use, and Ion Torrent PGM plugin for customer use. Trained machine learning models on high throughput sequencing to optimize probe design. Worked with team to achieve CE mark for HAI BioDetection kit and software. Inventor or co-inventor for seven patent applications.

Postdoctoral Associate, Computational Genomics Research Group and SysCODE Project (June 2009 - April 2011) Studies directed differentiation of embryonic stem cells into pancreatic cells. Developed genetic regulatory network algorithms and tools for ChIP-Seq and DNase-seq.

Graduate Student, Computational Genomics Research Group, MIT (January 2003 - May 2009) Research focused on ChIP-Chip data, microarray design, genetic regulatory network discovery, and computational tools for biology collaborators. Developed a novel method to identify transcription factor binding sites (Joint Binding Deconvolution). Expanded research group's computational infrastructure to include a compute cluster and Oracle databases for microarray and short-read sequencing data. Thesis project required experiment design and computational analysis to develop a novel technique to detect insertions, deletions, and inversions in nucleic acid samples.

Whitehead Institute Center for Genome Research (January 1998 - August 2002) Implemented a variety of laboratory information management and analysis systems for the Functional

Genomics Group. Developed programming tools for rapid development of workflow systems as Master of Engineering thesis project. Database development for SNP discovery project.

Education

Ph.D. Computer Science. MIT, June 2009. *Ruler Arrays Detect Genomic Insertions and Deletions*. Supervised by Profs. David Gifford, Gerry Fink, Tommi Jaakkola, and Ernest Fraenkel.

M.Eng. Computer Science. MIT, June 2002. *Code Versioning in a Workflow Management System*. Supervised by Prof. Michael Ernst.

S.B. Computer Science. MIT, June 2001.

Skills

- Developing and leading computational groups - hiring, onboarding, training, development, collaboration across R&D functions
- Computational biology methods for gene expression analysis, including alignment, QC, differential expression, signature generation, patient subgroup identification, and biomarker selection
- Data strategy and infrastructure for R&D including FAIR principle implementation and self-service analytics/visualization
- Extensive R, Java, Python, shell scripting, Scheme, Perl, and SQL programming experience
- Experience with the design and implementation of scalable scientific computing systems using Amazon Web Services.
- Assay development and regulatory approval
- Twenty-five years experience with biological and genomic datasets
- Extensive Linux, Unix, and Oracle administration experience
- Experience with git, GitLab, svn, CVS, RCS, make, and other software engineering tools.

Publications

Journal Articles

M. Studham, C. Vazquez-Mateo, E. Samy, P. Haselmayer, A. Aydemir, P. A. Rolfe, J. T. Merrill, E. F. Morand, J. DeMartino, A. Kao, and R. Townsend, **Identifying lupus Patient Subsets Through Immune Cell Deconvolution of Gene Expression Data in Two Atacisept Phase II Studies**, *ACR Open Rheumatology*, vol. 5, no. 10, pp. 536–546, 2023

I. Kalatskaya, G. Giovannoni, T. Leist, J. Cerra, U. Boschert, and P. A. Rolfe, **Revealing the immune cell subtype reconstitution profile in patients from the CLARITY study using deconvolution algorithms after cladribine tablets treatment**, *Scientific Reports*, vol. 13, no. 8067, 2023

- A. Spira, A. Awada, N. Isambert, D. Lorente, N. Penel, Y. Zhang, L. S. Ojalvo, C. Hicking, P. A. Rolfe, C. Ihling, I. Dussault, G. Locke, and C. Borel, **Identification of HMG2 as a predictive biomarker of response to bintrafusp alfa in a phase 1 trial in patients with advanced triple-negative breast cancer**, *Frontiers in Oncology*, vol. 12, 2022,
- Y. Vugmeyster, G. Locke, C. Helwig, P. A. Rolfe, J. Q. Dong, and K. Venkatakrishnan, **Risk assessment of drug–drug interaction potential for bintrafusp alfa with cytochrome P4503A4 substrates: A totality of evidence approach**, *Clinical and Translational Science*, 2022
- E. Strack, P. A. Rolfe, A. F. Fink, K. Bankov, T. Schmid, C. Solbach, R. Savai, W. Sha, L. Pradel, S. Hartmann, B. Brüne, and A. Weigert, **Identification of tumor-associated macrophage subsets that are associated with breast cancer prognosis**, *Clinical and Translational Medicine*, 2020
- J. Strauss, M. E. Gatti-Mays, B. C. Cho, A. Hill, S. Salas, E. McClay, J. M. Redman, H. A. Sater, R. N. Donahue, C. Jochems, E. Lamping, A. Burmeister, J. L. Marte, L. M. Cordes, M. Bilusic, F. Karzai, J. Ojalvo, G. Jehl, P. A. Rolfe, C. S. Hinrichs, R. A. Madan, J. Schlom, and J. L. Gulley, **Bintrafusp alfa, a bifunctional fusion protein targeting TGF- β and PD-L1, in patients with human papillomavirus-associated malignancies**, *Journal for Immunotherapy of Cancer*, vol. 8, December 2020
- V. Chelliah, G. Lazarou, S. Bhatnagar, J. P. Gibbs, M. Nijsen, A. Ray, B. Stoll, R. A. Thompson, A. Gulati, S. Soukharev, A. Yamada, J. Weddell, H. Sayama, M. Oishi, S. Wittemer-Rump, C. Patel, C. Niederalt, R. Burghaus, C. Scheerans, J. Lippert, S. Kabilan, I. Kareva, N. Belousova, A. Rolfe, A. Zutshi, M. Chenel, F. Venezia, S. Fouliard, H. Oberwittler, A. Scholer-Dahirel, H. Lelievre, D. Bottino, S. C. Collins, H. Q. Nguyen, H. Wang, T. Yoneyama, A. Z. Zhu, P. H. van der Graaf, and A. M. Kierzek, **Quantitative Systems Pharmacology Approaches for Immuno-Oncology: Adding Virtual Patients to the Development Paradigm**, *Clinical Pharmacology & Therapeutics*, 2020
- B. C. Cho, A. Daste, A. Ravaud, S. Salas, N. Isambert, E. McClay, A. Awada, C. Borel, J. Gulley, L. Ojalvo, C. Helwig, P. A. Rolfe, and N. Penel, **M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF- β , in patients (pts) with advanced SCCHN: Results from a phase I cohort**, *Annals of Oncology*, vol. 29, no. suppl 8, p. mdy287.004, 2018
- C. Ihling, B. Naughton, Y. Zhang, P. A. Rolfe, E. Frick-krieger, L. M. Terracciano, and I. Dussault, **Observational Study of PD-L1, TGF- β , and Immune Cell Infiltrates in Hepatocellular Carcinoma**, *Frontiers in Medicine*, vol. 6, no. February, pp. 1–9, 2019
- M. Schröder, M. Krötschel, L. Conrad, S. K. Naumann, C. Bachran, A. Rolfe, V. Umansky, L. Helming, and L. K. Swee, **Genetic screen in myeloid cells identifies TNF- α autocrine secretion as a factor increasing MDSC suppressive activity via Nos2 up-regulation**, *Scientific Reports*, vol. 8, no. 1, pp. 1–12, 2018
- S. Okitsu, M. Genest, N. Lewis, E. Tzvetkov, Y. Wu, A. Bender, A. Arazi, T. Eisenhaure, E. Browne, A. Rolfe, J. Derry, W. P. III, N. Hacohen, J. DeMartino, and J. Vlach, **A Novel Role for Galectin-3 Binding Protein in B Cell Biology and Antibody Secretion**, No. 69, ACR/ARHP, September 2017

- C. Xu, Y. Zhang, P. Alexander Rolfe, V. M. Hernández, W. Guzman, G. Kradjian, B. Marelli, G. Qin, J. Qi, H. Wang, H. Yu, R. Tighe, K. M. Lo, J. M. English, L. Radvanyi, and Y. Lan, **Combination therapy with NHS-muLL12 and avelumab (anti-PD-L1) enhances antitumor efficacy in preclinical cancer models**, *Clinical Cancer Research*, vol. 23, no. 19, pp. 5869–5880, 2017
- J. Veenemans, I. T. Overdeest, E. Snelders, I. Willemsen, Y. Hendriks, A. Adesokan, G. Doran, S. Brusio, A. Rolfe, A. Pettersson, and J. A. J. W. Kluytmans, **Next-generation sequencing for typing and detection of resistance genes: performance of a new commercial method during an outbreak of extended-spectrum-beta-lactamase-producing *Escherichia coli*.**, *J Clin Microbiol*, vol. 52, June 2014
- F. Arena, P. A. Rolfe, G. Doran, V. Conte, S. Gruszka, T. Clarke, Y. Adesokan, T. Giani, and G. M. Rossolini, **Rapid resistome fingerprinting and clonal lineage profiling of carbapenem-resistant *Klebsiella pneumoniae* isolates by targeted next-generation sequencing.**, *J Clin Microbiol*, vol. 52, February 2014
- J. W. Koehler, A. T. Hall, P. A. Rolfe, A. N. Honko, G. F. Palacios, J. N. Fair, J.-J. Muyembe, P. Mulembekani, R. J. Schoepp, A. Adesokan, and T. D. Minogue, **Development and evaluation of a panel of filovirus sequence capture probes for pathogen detection by next-generation sequencing.**, *PLoS One*, vol. 9, September 2014
- M. Arbab, S. Mahony, H. Cho, J. M. Chick, P. A. Rolfe, J. P. van Hoff, V. W. S. Morris, S. P. Gygi, R. L. Maas, D. K. Gifford, and R. I. Sherwood, **A multi-parametric flow cytometric assay to analyze DNA-protein interactions**, *Nucleic Acids Res*, vol. 41, January 2013
- P. A. Rolfe, D. A. Bernstein, P. Grisafi, G. R. Fink, and D. K. Gifford, **Ruler Arrays Reveal Haploid Genomic Structural Variation**, *PLoS One*, vol. 7, August 2012
- P. A. Rolfe and D. K. Gifford, **ReadDB provides efficient storage for mapped short reads.**, *BMC Bioinformatics*, vol. 12, p. 278, July 2011
- R. D. Dowell, O. Ryan, A. Jansen, D. Cheung, S. Agarwala, T. Danford, D. A. Bernstein, P. A. Rolfe, L. E. Heisler, B. Chin, C. Nislow, G. Giaever, P. C. Phillips, G. R. Fink, D. K. Gifford, and C. Boone, **Genotype to phenotype: a complex problem.**, *Science*, vol. 328, p. 469, April 2010
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D. T. Odom, R. D. Dowell, E. S. Jacobsen, L. Nekludova, P. A. Rolfe, T. W. Danford, D. K. Gifford, E. Fraenkel, G. I. Bell, and R. A. Young, **Core transcriptional regulatory circuitry in human hepatocytes.**, *Mol Syst Biol*, vol. 2, p. 2006.0017, June 2006

Y. Qi, A. Rolfe, K. D. MacIsaac, G. K. Gerber, D. Pokholok, J. Zeitlinger, T. Danford, R. D. Dowell, E. Fraenkel, T. S. Jaakkola, R. A. Young, and D. K. Gifford, **High-resolution computational models of genome binding events.**, *Nat Biotechnol*, vol. 24, pp. 963–70, August 2006

D. K. Pokholok, C. T. Harbison, S. Levine, M. Cole, N. M. Hannett, T. I. Lee, G. W. Bell, K. Walker, P. A. Rolfe, E. Herbolsheimer, J. Zeitlinger, F. Lewitter, D. K. Gifford, and R. A. Young, **Genome-wide map of nucleosome acetylation and methylation in yeast.**, *Cell*, vol. 122, pp. 517–27, August 2005

D. T. Odom, N. Zizlsperger, D. B. Gordon, G. W. Bell, N. J. Rinaldi, H. L. Murray, T. L. Volkert, J. Schreiber, P. A. Rolfe, D. K. Gifford, E. Fraenkel, G. I. Bell, and R. A. Young, **Control of pancreas and liver gene expression by HNF transcription factors.**, *Science*, vol. 303, pp. 1378–81, February 2004

F. Robert, D. K. Pokholok, N. M. Hannett, N. J. Rinaldi, M. Chandy, A. Rolfe, J. L. Workman, D. K. Gifford, and R. A. Young, **Global position and recruitment of HATs and HDACs in the yeast genome.**, *Mol Cell*, vol. 16, pp. 199–209, October 2004

M. Cargill, D. Altshuler, J. Ireland, P. Sklar, K. Ardlie, N. Patil, N. Shaw, C. R. Lane, E. P. Lim, N. Kalyanaraman, J. Nemesh, L. Ziaugra, L. Friedland, A. Rolfe, J. Warrington, R. Lipschutz, G. Q. Daley, and E. S. Lander, **Characterization of single-nucleotide polymorphisms in coding regions of human genes.**, *Nat Genet*, vol. 22, pp. 231–8, July 1999

Posters and Abstracts

J. Merrill, M. Studham, E. Morand, A. Aydemir, C. M. Vazquez, A. Rolfe, A. Kao, and R. Townsend, **Identifying an SLE Patient Cluster with Greater Treatment Effect: Immune Cell Deconvolution of Gene Expression in Two Atacisept Phase II Studies**, No. 0866, American College of Rheumatology, November 2020. ACR Convergence 2020

G. Locke, Y. Zhang, L. S. Ojalvo, C. Helwig, A. Rolfe, O. Christensen, and I. Dussault, **Abstract P3-09-13: Identification of a tumor biomarker in advanced triple-negative breast cancer that predicts response to bintrafusp alfa (M7824), a bifunctional fusion protein targeting transforming growth factor- β and programmed death ligand 1**, AACR, 2020

I. Kalatskaya, G. Giovannoni, T. Leist, P. S. Sorensen, U. Boschert, J. Demartino, and A. Rolfe, **Revealing the Immune Cell Subtype Reconstitution Profile in Cladribine Treated Patients at the 96 Week Timepoint (CLARITY) Using Deconvolution Algorithms (1520)**, AAN, 2020

G. Giovannoni, T. Leist, P. S. Sorensen, I. Kalatskaya, U. Boschert, J. DeMartino, and A. Rolfe, **Increase of Naive B Cells, M2 Macrophages and Reduction of Memory B/T Cells During Immune Repopulation at 96 Weeks in CLARITY Assessed by Immune Cell Deconvolution**, *Multiple Sclerosis Journal*, vol. 25, no. 2 suppl, pp. 357–580, 2019

P. Shah, J. Kaczmarzyk, A. Myronov, K. Gruba, and A. Rolfe, **Understanding contribution and independence of multiple biomarkers for predicting response to atezolizumab**, American Society of Clinical Oncology, 2019

J. Strauss, M. E. Gatti-Mays, B. Cho, S. Salas, E. McClay, J. Redman, H. A. Sater, R. N. Donahue, E. Lamping, A. Burmeister, *et al.*, **Abstract CT075: Phase I evaluation of M7824, a bifunctional fusion protein targeting TGF- β and PD-L1, in patients with human papillomavirus (HPV)-associated malignancies**, AACR, 2019

E. Samy, M. Studham, A. Kao, P. Haselmayer, P. Chang, A. Rolfe, D. Wofsy, J. DeMartino, and R. Townsend, **Identifying lupus patient subsets and specific pharmacodynamic changes through immune cell deconvolution of gene expression data in atacicept-treated patients in the APRIL-SLE study**, *Lupus Science & Medicine*, vol. 6, no. Suppl 1, pp. A158–A158, 2019

A. M. Deshpande, R. Fontana, Y. Zhang, M. Ruisi, D. Zhang, T. Senger, and P. A. Rolfe, **Galectin-9 drives TIM-3 mediated immune suppression**, vol. 78 of *AACR Annual Meeting*, AACR, July 2018

C. Ihling, S. Yoast, Y. Zhang, B. Naughton, M. Urban, P. A. Rolfe, E. Frick-Krieger, and I. Dus-sault, **Characterization of PD-L1 expression and the immune cell microenvironment in hepatocellular carcinoma (HCC) and non-cirrhotic liver tissue adjacent to HCC**, vol. 77, AACR, July 2017

Patent Applications

P. A. Rolfe, **WO 2013067167 A3: Method and system for detection of an organism**. US Patent Application, 2011

P. A. Rolfe, **WO 2013040060 A3: Nucleic acids for multiplex detection of hepatitis c virus**. US Patent Application, 2011

L. Diamond, J. Kumm, and P. A. Rolfe, **WO 2011156795 A3: Nucleic acids for multiplex organism detection and methods of use and making the same**. US Patent Application, 2011

D. K. Gifford and P. A. Rolfe, **US Patent Application 20100304990: Ruler Arrays**. US Patent Application, 2008

Research Interests

- Application of machine learning to pharmaceutical development and biology
- Genome plasticity: evolution and diversity within an individual
- Mechanisms of auto-immune disease to understand routes to cure vs treatment of symptoms
- Development of new uses for high throughput sequencing and single-cell technologies