

## *Curriculum Vitae*

### Floyd Eric Romesberg

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#### Education

<i>Description</i>	<i>Date</i>	<i>Location</i>	<i>Advisor</i>
Postdoctoral Studies	1994– 1998	UC Berkeley, Berkeley, CA	Professor Peter G. Schultz
Ph.D. in Chemistry	1994	Cornell University, Ithaca, NY	Professor David B. Collum
M.S. in Chemistry	1990	Cornell University, Ithaca, NY	Professor David B. Collum
B.S. in Chemistry	1988	Ohio State University, Columbus, OH	Professor Matthew S. Platz

#### Appointments

2019 – present	Distinguished Fellow, Synthorx
2014 – 2019	Professor, Department of Chemistry, The Scripps Research Institute
2006 – 2014	Associate Professor, Department of Chemistry, The Scripps Research Institute
1998 – 2006	Assistant Professor, Department of Chemistry, The Scripps Research Institute

#### Professional Experience

2014 – 2019	Synthorx, La Jolla, CA (Scientific Founder, Consultant, Board of Directors);
2010 – 2013	RQx Pharmaceuticals, Inc., La Jolla, CA (Scientific Founder, Consultant, SAB member); Acquired by Genentech in 2013
2005 – 2011	Achaogen Inc., South San Francisco, CA (Scientific Founder, Consultant, SAB member); NASDAQ: AKAO

#### Honors

2020	Fellow, National Academy of Inventors
2018	ACS San Diego Section Distinguished Scientist Award
2018	Royal Society of Chemistry Bioorganic Chemistry Award
2015	ACS Nobel Laureate Signature Award for Graduate Education in Chemistry
2008 – 2009	Member, Institute for Defense Analysis, Defense Science Study Group
2005	World Technology Award Nominee in Biotechnology
2004	Discover Magazine Technology Innovation Award
2004	NSF CAREER Award
2003	Camille Dreyfus Teacher Scholar Award
2003	Susan B. Komen Breast Cancer Foundation Award
2002	The Baxter Foundation Award
1994 – 1996	NIH National Research Service Award Postdoctoral Fellowship
1987	The Mac Nevin Award

**Publications, *electronic list* via PubMed: <http://bit.ly/2uEWtff>**

**Publications: Principal Investigator, Primary Research Articles**

1. EC Fischer, K Hashimoto, Y Zhang, AW Feldman, VT Dien, RJ Karadeema, R Adhikary, MP Ledbetter, R Krishnamurthy, **FE Romesberg** (2020) New codons for efficient production of unnatural proteins in a semi-synthetic organism, *Nat Chem Biol* 16:570–576.
2. MP Ledbetter, JM Craig, RJ Karadeema, MT Noakes, HC Kim, SJ Abell, JR Huang, BA Anderson, R Krishnamurthy, JH Gundlach, **FE Romesberg** (2020) Nanopore sequencing of an expanded genetic alphabet reveals high-fidelity replication of a predominantly hydrophobic unnatural base pair, *J Am Chem Soc* 142:2110–2114.
3. Q Shao, T Chen, K Sheng, Z Liu, Z Zhang, **FE Romesberg** (2020) Selection of aptamers with large hydrophobic 2'-substituents, *J Am Chem Soc* 142:2125–2128.
4. AX Zhou, K Sheng, AW Feldman, **FE Romesberg** (2019) Progress toward eukaryotic semisynthetic organisms: translation of unnatural codons, *J Am Chem Soc* 141:20166–20170.
5. SI Walsh, DS Peters, PA Smith, A Craney, MM Dix, BF Cravatt, **FE Romesberg** (2019) Inhibition of protein secretion in *Escherichia coli* and sub-MIC effects of arylomycin antibiotics, *Antimicrob Agents Chemother* 63:e01253-18.
6. R Adhikary, J Zimmermann, RL Stanfield, IA Wilson, W Yu, M Oda, **FE Romesberg** (2019) Structure and dynamics of stacking interactions in an antibody binding site, *Biochemistry* 58:2987-2995.
7. AW Feldman, VT Dien, RJ Karadeema, EC Fischer, Y You, BA Anderson, R Krishnamurthy, JS Chen, L Li, **FE Romesberg** (2019) Optimization of replication, transcription, and translation in a semi-synthetic organism. *J Am Chem Soc* 141:10644-10653.
8. VT Dien, M Holcomb, AW Feldman, EC Fischer, TJ Dwyer, **FE Romesberg** (2018) Progress toward a semi-synthetic organism with an unrestricted expanded genetic alphabet, *J Am Chem Soc* 140:16115-16123
9. CH Yeh, SI Walsh, A Craney, MG Tabor, AF Voica, R Adhikary, SE Morris, **FE Romesberg** (2018) Optimization of a  $\beta$ -lactam scaffold for antibacterial activity via the inhibition of bacterial type I signal peptidase, *ACS Med Chem Lett* 4:376-380
10. AW Feldman, EC Fischer, MP Ledbetter, J-Y Liao, JC Chaput, **FE Romesberg** (2018) A tool for the import of natural and unnatural nucleoside triphosphates into bacteria, *J Am Chem Soc* 140:1447-1454
11. DS Peters, **FE Romesberg**, PS Baran (2018) Scalable access to arylomycins via C-H functionalization logic, *J Am Chem Soc* 140:2072-2075
12. M Holcomb, R Adhikary, J Zimmermann, **FE Romesberg** (2018) Topological evidence of previously overlooked  $N_{i+1}-H \cdots N_i$  H-bonds and their contribution to protein structure and stability, *J Phys Chem A* 122:446-450
13. MP Ledbetter, RJ Karadeema, **FE Romesberg** (2018) Reprogramming the replisome of a semisynthetic organism for the expansion of the genetic alphabet, *J Am Chem Soc* 140:758-765
14. Y Zhang, JL Ptacin, EC Fischer, HR Aerni, CE Caffaro, K San Jose, AW Feldman, CR Turner, **FE Romesberg** (2017) A semi-synthetic organism that stores and retrieves increased genetic information, *Nature* 551:644-647
15. A Craney, **FE Romesberg** (2017) Stable signal peptides and the response to secretion stress in *Staphylococcus aureus*, *mBio* 8:e01507-17
16. Z Liu, T Chen, **FE Romesberg** (2017) Evolved polymerases facilitate selection of fully 2'OMe-modified aptamers, *Chem Sci* 8:8179-8182
17. T Chen, **FE Romesberg** (2017) Enzymatic synthesis, amplification, and application of DNA with a functionalized backbone, *Angew Chem Int Ed* 56:14046-14051
18. AW Feldman, **FE Romesberg** (2017) In vivo structure-activity relationships and optimization of an unnatural base pair for replication in a semi-synthetic organism, *J Am Chem Soc* 139:11427-11433
19. T Chen, **FE Romesberg** (2017) Polymerase chain transcription: exponential synthesis of RNA and modified RNA, *J Am Chem Soc* 139:9949-9954

20. SE Morris, AW Feldman, **FE Romesberg** (2017) Synthetic biology parts for the storage of increased genetic information in cells, *ACS Synth Biol*, 6:1834-1840
21. R Adhikary, YX Tan, J Liu, J Zimmermann, M Holcomb, C Yvellez, PE Dawson, **FE Romesberg** (2017) Conformational heterogeneity and DNA recognition by the morphogen bicoid, *Biochemistry* (ACS Editors' Choice) 56:2787-2793
22. D Thirunavukarasu, T Chen, Z Liu, N Hongdilokkul, **FE Romesberg** (2017) Selection of 2'-fluoro-modified aptamers with optimized properties, *J Am Chem Soc (Comm)* 139:2892-2895
23. AW Feldman, VT Dien, **FE Romesberg** (2017) Chemical stabilization of unnatural nucleotide triphosphates for the in vivo expansion of the genetic alphabet, *J Am Chem Soc* 139:2464-2647
24. Y Zhang, BM Lamb, AW Feldman, AX Zhou, T Lavergne, L Li, **FE Romesberg** (2017) A semisynthetic organism engineered for the stable expansion of the genetic alphabet, *Proc Natl Acad Sci USA* 114:1317-1322
25. R Adhikary, J Zimmermann, **FE Romesberg** (2017) Transparent window vibrational probes for the characterization of proteins with high structural and temporal resolution, *Chem Rev* 117:1927-1969
26. T Chen, N Hongdilokkul, Z Liu, D Thirunavukarasu, **FE Romesberg** (2016) The expanding world of DNA and RNA, *Curr Op Chem Biol* 34:80-87
27. T Chen, N Hongdilokkul, Z Liu, R Adhikary, SS Tsuen, **FE Romesberg** (2016) Evolution of thermophilic DNA polymerases for the recognition and amplification of C2'-modified DNA, *Nat Chem* 8:556-562
28. T Lavergne, R Lamichhane, DA Malyshev, Z Li, L Li, E Sperling, JR Williamson, DP Millar, **FE Romesberg** (2016) FRET characterization of complex conformational changes in a large 16S ribosomal RNA fragment site-specifically labeled using unnatural base pairs, *ACS Chem Biol* 11:1347-1353
29. R Adhikary, J Zimmermann, PE Dawson, **FE Romesberg** (2015) The temperature dependence of CN and SCN IR absorptions facilitates their interpretation and use as probes of proteins, *Anal. Chem.* 87:11561-11567
30. A Craney, MM Dix, R Adhikary, BF Cravatt, **FE Romesberg** (2015) An alternative terminal step of the general secretory pathway in *Staphylococcus aureus*, *mBio*. 6:e01178-15
31. DB Steed, J Liu, E Wasbrough, L Miller, S Halasohoris, J Miller, B Somerville, JR Hershfield, **FE Romesberg** (2015) Origins of *Y. pestis* sensitivity to the arylomycin antibiotics and the inhibition of type I signal peptidase, *Antimicrob. Agents Chemother.* 59:3887-3898
32. A Craney, **FE Romesberg** (2015) A putative Cro-like repressor contributes to arylomycin resistance in *Staphylococcus aureus*, *Antimicrob. Agents Chemother.* 59:3066-3074
33. RA Adhikary, W Yu, M Oda, T Chen, R Walker, R Stanfield, I Wilson, J Zimmermann, **FE Romesberg** (2015) Adaptive mutations alter antibody structure and dynamics during affinity maturation, *Biochemistry* 54:2085-2093
34. RA Rodriguez, DB Steed, Y Kawamata, S Su, PA Smith, TC Steed, **FE Romesberg**, PS Baran (2014) Axinellamines as broad-spectrum antibacterial agents: scalable synthesis and biology, *J Am Chem Soc* 136:15403-15413
35. R Adhikary, J Zimmermann, J Liu, RP Forrest, TD Janicki, PE Dawson, SA Corcelli, **FE Romesberg** (2014) Evidence of an unusual N-H...N hydrogen bond in proteins, *J Am Chem Soc* 136:13474-13477
36. K Dhami, DA Malyshev, P Ordoukhanian, T Kubelka, M Hocek, **FE Romesberg** (2014) Systematic exploration of a class of hydrophobic unnatural base pairs yields multiple new candidates for the expansion of the genetic alphabet, *Nucleic Acids Res* 42:10235-10244
37. DA Malyshev, K Dhami, T Lavergne, T Chen, N Dai, JM Foster, IR Corrêa, **FE Romesberg** (2014) A semi-synthetic organism with an expanded genetic alphabet, *Nature* 509:385-388 [featured on the cover]
38. R Adhikary, J Zimmermann, PE Dawson, **FE Romesberg** (2014) IR probes of protein microenvironments: utility and potential for perturbation, *ChemPhysChem* 15:849-853
39. L Li, M Degardin, T Lavergne, DA Malyshev, K Dhami, P Ordoukhanian, **FE Romesberg** (2014) Natural-like replication of an unnatural base pair for the expansion of the genetic alphabet and biotechnology applications, *J Am Chem Soc* 136:826-829 [cover story]

40. K Betz, DA Malyshev, T Lavergne, W Welte, K Diederichs, **FE Romesberg**, A Marx (2013) Structural insights into DNA replication without hydrogen bonds, *J Am Chem Soc* 135:18637-18643
41. J Liu, PA Smith, DB Steed, **FE Romesberg** (2013) Efforts toward broadening the spectrum of arylomycin antibiotic activity, *Bioorg Med Chem Lett* 23:5654-5659
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43. R Adhikary, J Zimmermann, J Liu, PE Dawson, **FE Romesberg** (2013) Experimental characterization of electrostatic and conformational heterogeneity in an SH3 domain, *J Phys Chem B* 117:13082-13089
44. T Lavergne, M Degardin, DA Malyshev, HT Quach, K Dhami, P Ordoukhanian, **FE Romesberg** (2013) Expanding the scope of replicable unnatural DNA: stepwise optimization of a predominantly hydrophobic base pair, *J Am Chem Soc* 135:5408-5419
45. D Quinto-Aleman, A Canerina-Amaro, LG Hernandez-Abad, F Machin, **FE Romesberg**, C Gil-Lamaignere (2012) Yeasts acquire resistance secondary to antifungal drug treatment by adaptive mutagenesis, *PLoS One*, 7:e42279
46. DA Malyshev, K Dhami, HT Quach, T Lavergne, P Ordoukhanian, A Torkamani, **FE Romesberg** (2012) Efficient and sequence-independent replication of DNA containing a third base pair establishes a functional six letter genetic alphabet, *Proc Natl Acad Sci USA*, 109:12005-12010
47. PA Smith, **FE Romesberg** (2012) Mechanism of action of the arylomycin antibiotics and the effects of signal peptidase I inhibition *Antimicrob Agents Chemother*, 56:5054-5060
48. R Adhikary, W Yu, M Oda, J Zimmermann, **FE Romesberg** (2012) Protein dynamics and the diversity of an antibody response, *J Biol Chem* 287:27139-27147
49. K Betz, DA Malyshev, T Lavergne, W Welte, K Diederichs, TJ Dwyer, P Ordoukhanian, **FE Romesberg**, A Marx (2012) KlenTaq polymerase replicates unnatural base pairs by inducing a Watson-Crick geometry, *Nat Chem Biol*, 8:612-614
50. W Yu, PE Dawson, J Zimmermann, **FE Romesberg** (2012) Carbon-deuterium bonds as probes of protein thermal unfolding, *J Phys Chem B*, 116:6397-6403
51. MA Schallenberger, S Niessen, C Shao, B J Fowler, **FE Romesberg** (2012) Type I signal peptidase and protein secretion in *Staphylococcus aureus*, *J Bacteriol* 194:2677-2686
52. T Lavergne, DA Malyshev, **FE Romesberg** (2012) Major groove substituents and polymerase recognition of a class of unnatural base pairs, *Chem Eur J* 18:1231-1239
53. YJ Seo, DA Malyshev, T Lavergne, P Ordoukhanian, **FE Romesberg** (2011) Site-specific labeling of DNA and RNA using an efficiently replicated and transcribed class of unnatural base pairs, *J Am Chem Soc* 133:19878-19888
54. J Liu, C Luo, PA Smith, JK Chin, MGP Page, M Paetzl, **FE Romesberg** (2011) Synthesis and characterization of the arylomycin lipoglycopeptide antibiotics and the crystallographic analysis of their complex with signal peptidase, *J Am Chem Soc* 133:17869-17872
55. KC Nicolaou, SP Ellery, F Rivas, K Saye, E Rogers, TJ Workinger, M Schallenberger, R Tawatao, A Montero, A Hessell, **F Romesberg**, D Carson, D Burton (2011) Synthesis and biological evaluation of 2',4'- and 3',4'- bridged nucleoside analogues, *Bioorg Med Chem* 19:5648-5669
56. J Zimmermann, MC Thielges, YJ Seo, PE Dawson, **FE Romesberg** (2011) Cyano groups as probes of protein microenvironments and dynamics, *Angew Chem Int Ed* 50:8333-8337
57. TC Roberts, M Schallenberger, J Liu, PA Smith, **FE Romesberg** (2011) Initial efforts toward the optimization of arylomycins for antibiotic activity, *J Med Chem* 54:4954-4963
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60. PA Smith, ME Powers, TC Roberts, **FE Romesberg** (2011) *In vitro* activities of arylomycin natural-product antibiotics against *Staphylococcus epidermidis* and other coagulase-negative Staphylococci, *Antimicrob*



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63. MA Schallenberger, T Newhouse, PS Baran, **FE Romesberg** (2010) The psychotrimine natural products have antibacterial activity against Gram-positive bacteria and act via membrane disruption, *J Antibiot (Tokyo)* 63:685-687
64. DA Malyshev, DA Pfaff, SI Ippoliti, GT Hwang, TJ Dwyer, **FE Romesberg** (2010) Solution structure, mechanism of replication, and optimization of an unnatural base pair, *Chem Eur J* 16:12650-12659
65. B Li, P Smith, DJ Horvath, Jr, **FE Romesberg**, SS Justice (2010) SOS regulatory elements are essential for UPEC pathogenesis, *Microbes Infect* 12:662-668
66. AM Leconte, MP Patel, LE Sass, P McInerney, M Jarosz, L Kung, J L Bowers, PR Buzby, JW Efcavitch, **FE Romesberg** (2010) Directed evolution of DNA polymerases for next-generation sequencing, *Angew Chem Int Ed Engl* 49:5921-5924
67. D Chen, L Lei, C Lu, R Flores, MP DeLisa, TC Roberts, **FE Romesberg**, G Zhong (2010) Secretion of the chlamydial virulence factor CPAF requires the Sec-dependent pathway, *Microbiology* 156:3031-3040
68. J Zimmermann, **FE Romesberg**, CL Brooks, 3rd, IF Thorpe (2010) Molecular description of flexibility in an antibody combining site, *J Phys Chem B* 114:7359-7370
69. P Weinkam, J Zimmermann, **FE Romesberg**, PG Wolynes (2010) The folding energy landscape and free energy excitations of cytochrome *c*, *Acc Chem Res* 43:652-660
70. D Malyshev, YJ Seo, P Ordoukhanian, **FE Romesberg** (2009) PCR with an expanded genetic alphabet, *J Am Chem Soc* 131:14620-14621
71. YJ Seo, **FE Romesberg** (2009) Major groove derivatization of an unnatural base pair, *ChemBioChem* 10:2394-2400 [cover story]
72. GT Hwang, Y Hari, **FE Romesberg** (2009) The effects of unnatural base pairs and mismatches on DNA duplex stability and solvation *Nucleic Acids Res* 37:4757-4763
73. J Zimmermann, K Gundogdu, ME Cremeens, JN Bandaria, GT Hwang, MC Thielges, CM Cheatum, **FE Romesberg** (2009) Efforts toward developing probes of protein dynamics: vibrational dephasing and relaxation of carbon-deuterium stretching modes in deuterated leucine *J Phys Chem B* 113:7991-7994
74. DA Harris, M E Powers, **FE Romesberg** (2009) Synthesis and biological evaluation of penem inhibitors of bacterial signal peptidase *Bioorg Med Chem Lett* 19:3787-3790
75. ME Cremeens, J Zimmermann, W Yu, PE Dawson, **FE Romesberg** (2009) Direct observation of structural heterogeneity in a  $\beta$ -sheet, *J Am Chem Soc* 131:5726-5727
76. MC Thielges, J Zimmermann, **FE Romesberg** (2009) Direct observation of ligand dynamics in cytochrome *c*, *J Am Chem Soc* 131:6054-6055
77. YJ Seo, S Matsuda, **FE Romesberg** (2009) Transcription of an expanded genetic alphabet, *J Am Chem Soc* 131:5046-5047
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79. D Groff, MC Thielges, S Celliti, PG Schultz, **FE Romesberg** (2009) Efforts toward the direct experimental characterization of enzyme microenvironments: tyrosine 100 in dihydrofolate reductase, *Angew Chem, Int, Ed* 48:3478-3481
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83. P Weinkam, J Zimmermann, LB Sagle, S Matsuda, PE Dawson, PG Wolynes, **FE Romesberg** (2008) Characterization of alkaline transitions in ferricytochrome *c* using carbon-deuterium infrared probes,

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