Stéphane P. Roche, Ph.D.

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BORN: November 15, **1979** in France (US permanent resident)

RESEARCH INTERESTS

Synthetic Organic Chemistry, Reaction Design, Natural Product Synthesis, Biomimetic Synthesis, Chemical Biology and Drug Discovery.

EDUCATION

2008 – 2011	Postdoctoral Associate Boston University, Chemistry Department, Massachusetts, USA. *Mentor*: Prof. John Porco
2006 – 2008	Postdoctoral Associate @-STAR Institute of Chemical and Engineering Sciences (ICES) at Biopolis, Singapore. *Mentor*: Prof. K.C. Nicolaou
2002 – 2006	Ph.D. in Organic chemistry Blaise Pascal University, Clermont-Ferrand, France, **2006**. *Mentor*: Prof. David Aitken
2000 – 2002	M.S. in Organic Chemistry Blaise Pascal University, Clermont-Ferrand, France, **2002** (ranked: 1st out of 30) *Advisor*: Prof. S. Giorgi-Renault (University René Descartes, Paris V)
1997 - 2000	B.S. with Honors in Chemistry Blaise Pascal University, Clermont-Ferrand, France, **2000** (ranked: 4th out of 49)

PROFESSIONAL APPOINTMENTS

2018 – Present	Associate Professor Department of Chemistry and Biochemistry, FAU.
2015 – Present	Faculty Member Center for Molecular Biology and Biotechnology, FAU.
2011 – 2017	Assistant Professor Department of Chemistry and Biochemistry, FAU.

AWARDS

2014	Mentor and Mentee FAU Award with Prof. S. Lepore
2012	Mentor and Mentee FAU Award with Prof. S. Lepore
2006 – 2007	Postdoctoral Fellowship (SFC Auvergne; French Chemical Society)
2002 – 2005	French Government Merit Grant (Full scholarship for the PhD)

MEMBERSHIPS

2009 – Present	ACS (American Chemical Society)
2016 – 2018	AHA (American Heart Association)
2002 – 2006	SFC (French Chemical Society)

PUBLICATIONS & PATENTS

List of Independent Publications (names of FAU undergraduate coauthors are underlined)

1. Scesa, P.; **Roche, S. P.; West, L. M.** Enantiospecific Synthesis of (+)-Providencin and its Unexpected Regioisomer via a Biomimetic Norrish–Yang Cyclization from (–)-Bipinnatin E. Will be proposed to *Org. Lett.* **2022** (*finalized manuscript*)
2. Zaghouani, M.; Zhao, G.; Richaud, A. D.; Wangpaichitr, M.; Savaraj, N.; **Roche, S. P.** Bent to Bind: Exploiting the Programmed Death-1 Immunoreceptor Plasticity to Design β-Hairpin Inhibitors Mimics of Pembrolizumab. *ChemBioChem* **2022** (*manuscript under review*). Preprint *ChemRxiv*. DOI: 10.26434/chemrxiv.14477730.v1 *Link*
3. Scesa, P.; **West, L. M.**; **Roche, S. P.** Role of Macrocyclic Conformational Steering in a Kinetic Route toward Bielschowskysin. *J. Am. Chem. Soc.* **2021**, *143,* 7566–7577.
4. **Roche, S. P.** Recent Advances in Oxa-6π Electrocyclization Reactivity for the Synthesis of Privileged Natural Product Scaffolds. *Organics* **2021**, *2*, 376–387. *Link*
5. Richaud, A. D.; Zhao, G.; Hobloss, S.; **Roche, S. P.** Folding in Place: Design of β-Strap Motifs to Stabilize the Folding of Hairpins with Long Loops. *J. Org. Chem.* **2021**, *86,* 13535–13547; Preprint *ChemRxiv*. DOI: 10.26434/chemrxiv.12912452.v1
6. **Roche, S. P.** In the pursuit of (ald)imine surrogates for the direct asymmetric synthesis of non-proteinogenic α-amino acids. *Synthesis* **2021,** *53*, 2767–2776.
7. Richaud, A. D.; **Roche, S. P.** Structure–Property Relationship Study of *N*-(Hydroxy)Peptides for the Design of Self-Assembled Parallel *β*-Sheets. *J. Org. Chem.* **2020**, *19*, 12329–12342; Preprint *ChemRxiv*. DOI: 10.26434/chemrxiv.12486236.v1
8. Zhao, G.; Samanta, S. S.; Michieletto, J.; **Roche, S. P.** A Broad Substrate Scope of aza-Friedel−Crafts Alkylation for the Synthesis of Quaternary α-Amino Esters. *Org. Lett.* **2020**, 22, 5822–5827; Preprint *ChemRxiv*. DOI: 10.26434/chemrxiv.12111309.v1
9. Shearer, C.; Desaunay, O.; Zorc, S.; Richaud, A. D.; Samanta, S. S.; Jeedimalla, N.; **Roche, S. P.** Interrupted Knoevenagel Condensation for the Synthesis of Unsymmetrical Fused Tricyclic Dihydropyrans. *Tetrahedron* **2019**, 130606.
10. Samanta, S. S.; **Roche, S. P.** Synthesis and Reactivity of α-Haloglycine Esters: Hyperconjugation in Action. *Eur. J. Org. Chem.* **2019**, 6597–6605. ***Editor Choice Issue Cover:*** *Link*
11. Bendelsmith, A. J.; Kim, S. C.; Wasa, M.; **Roche, S. P.**; **Jacobsen, E. N**. Enantioselective Synthesis of α-Allyl Amino Esters via Hydrogen-Bond-Donor Catalysis. *J. Am. Chem. Soc.* **2019**, *141*, 11414–11419.
12. Zaghouani, M.; Bögeholz, L. A. K.; Mercier, E.; **Wintermeyer, W.**; **Roche, S. P.** Total synthesis of (±)-fumimycin and analogues for biological evaluation as peptide deformylase inhibitors. *Tetrahedron* **2019**, *75*, 3216–3230. ***Editor Invitation for the Tetrahedron Young Investigator Award Issue***. PMID: 31555018
13. **Lepir, T.**; Zaghouani, M.; **Roche, S. P.**; Li, Y. Y.; Suarez, M.; Irias, M. J.; Savaraj, N. Nivolumab to pembrolizumab switch induced a durable melanoma response: A case report. *Medicine*, **2019**, *98*, e13804-e13810. PMID:30633154
14. Jeedimalla, N.; Jacquet, C.; Bahneva, D.; Youte Tendoung, J.-J.; **Roche, S. P.** Synthesis of α-Arylated Cycloalkanones from Congested Trisubstituted Spiro-epoxides: Application of the House–Meinwald Rearrangement for Ring Expansion. *J. Org. Chem.* (full article) **2018**, *83*, 12357–12373. ***Editor Choice Selection and Issue Cover***. *Link* PMID: 30089202
15. Scesa, P.; Wangpaichitr, M.; Savaraj, N.; **West, L.**; **Roche, S. P.** A Kinetic Dearomatization Strategy for an Expedient Route to Bielschowskysin Skeleton. *Angew. Chem. Int. Ed.* **2018**, *57*, 1316–1321. ***Selected Hot Paper***. PMID: 29232501

16. Samanta, S. S.; **Roche, S. P.** In Situ-Generated Glycinyl Chloroaminals for a Verstatile One-Pot Synthesis of Non-Proteinogenic α-Amino Esters. *J. Org. Chem.* (full article) **2017**, *82*, 8514–8526. PMID: 28737944

17. Hall, A.; **Roche, S. P.; West, L.** Synthesis of Briarane Diterpenoids: Biomimetic Transannular Oxa-6π Electrocyclization Induced by a UVA/UVC Photoswitch. *Org. Lett.* **2017**, *19*, 576–579. PMID: 28080074

18. Roche, S. P.; Youte Tendoung, J.-J.; Tréguier, B. Advances in Dearomatization Strategies of Indoles *Tetrahedron* **2015**, *71*, 3549–3591.

19. Jeedimalla, N.; Flint, M.; Smith, L.; Haces, A.; **Minond, D.; Roche, S. P.** Multicomponent Assembly of 4-Aza-podophyllotoxins: A Fast Entry to Highly Selective and Potent Anti-Leukemic Agents. *Eur. J. Med. Chem.* **2015**, *106*, 167–179. PMID: 26547055

20. Tréguier, B.; **Roche, S. P.** A Double Annulative Cascade of Tryptophan Containing Peptides Triggered by Selectfluor®. *Org. Lett.* **2014**, 16, 278–281. PMID: 24328461

21. Roche, S. P.; Samanta, S. S.; Gosselin, M. M. J. Autocatalytic One Pot Orchestration for the Synthesis of α-Arylated α-Amino Esters. *Chem. Commun.* **2014**, *50*, 2632–2634. PMID: 24471165

22. Wasa, M.; Liu, R. Y.; **Roche, S. P.; Jacobsen, E. N.** *Asymmetric Mannich Synthesis of α-Amino Esters by Anion-Binding Catalysis. J. Am. Chem. Soc.* **2014**, *136*, 12872–12875. ***Highlighted in Synfacts, 2014, 11, 1205 by B. List and M. R. Monaco****.* PMID: 25178040

23. Jeedimalla, N.; Johns, J.; **Roche, S. P.** Mechanistic Investigation and Implications of a Sacrificial Aniline for the Tandem Cascade Synthesis of 4-Aza-podophyllotoxin Analogues. *Tetrahedron Lett.* **2013**, *54*, 5845–5848.

List of Doctoral and Postdoctoral Publications

24. Santagata, S.; Mendillo, M. L.; Tang, Y-C.; Perley, C. C.; Roche, S. P.; Kwon, H.; Koeva, M.; Subramanian, A.; Golub, T. R.; Amon, A.; Porco Jr., J. A.; **Whitesell, L; Lindquist, S**. Tight coordination of protein translation and heat shock factor 1 activation supports the anabolic malignant state. *Science* **2013**, *341*, 250–260. PMID: 23869022

25. Lajkiewicz, N. J.; Roche, S. P.; Gerard, B., **Porco Jr., J. A.** Enantioselective Photocycloaddition of 3-Hydroxyflavones: Total Syntheses and Absolute Configuration Assignments of (+)-Ponapensin and (+)-Elliptifoline. *J. Am. Chem. Soc.* **2012**, *134*, 13108–13113. PMID: 22804454

26. Rodrigo, C. M.; Cencic, R.; Roche, S. P.; **Pelletier, J.; Porco Jr., J. A.** Synthesis of Rocaglamide Hydroxamates and Related Compounds as Eukaryotic Translation Inhibitors: Synthetic and Biological Studies. *J. Med. Chem.* **2012**, *55*, 558–562. PMID: 22128783

27. Roche, S. P.; **Porco Jr., J. A**. Dearomatization Strategies in Complex Natural Product Synthesis. *Angew. Chem. Int. Ed.* **2011**, *50*, 4068**–**4093. ***Review***:

28. Porco Jr., J. A.; Pelletier, J.; Roche, S. P.; Cencic, R.; Rodrigo, C. PCT Int. Appl. (**2011**), WO 2011140334 A2 20111110 ***Patent***

29. Teyssot, M-L.; Jarrousse, A-S.; Manin, M.; Chevry, A.; Roche, S.; Norre, F.; Beaudoin, C.; Morel, L.; Boyer, D.; Mahiou, R.; **Gautier, A.** Metal-NHC complexes: a survey of anti-cancer properties. *Dalton Trans.* **2009**, 6894–6902**.**

30. Roche, S. P.; Teyssot, M-L.; **Gautier, A.** Synthesis of 1,2 Diamines under Environmentally Benign Conditions: Application for the Preparation of Imidazolidiniums. *Tetrahedron Lett.* **2010,** 51, 1265**–**1268**.**

31. Roche, S. P.; Aitken, D. J. Chemistry of 4-Hydroxy-2-cyclopentenone derivatives. *Eur. J. Org. Chem.* **2010**, 5339–5358. ***Review***: ***Joined corresponding author***

32. Roche, S. P.; Cencic, R.; Pelletier, J.; **Porco, Jr., J. A.** Biomimetic Photocycloaddition of 3-Hydroxyflavones: Synthesis and Evaluation of Rocaglate Derivatives as Inhibitors of Eukaryotic Translation. *Angew. Chem. Int. Ed.* **2010**, *49*, 6533–6538*.* PMID: 20687060

33. Faure, S.; Hjelmgaard, T.; Roche, S. P.; **Aitken, D. J**. Passerini Reaction-Amine Deprotection-Acyl Migration Peptide Assembly: Efficient Formal Synthesis of Cyclotheonamide C. *Org. Lett.* **2009***, 11,* 1167–1170. PMID:1 9203293

34. Roche, S. P.; Faure, S.; **Aitken, D. J.** Total Synthesis of Cyclotheonamide C using a Tandem Backbone-Extension–Coupling Methodology. *Angew. Chem. Int. Ed.* **2008**, *47*, 6840–6842. PMID: 18661464

35. Roche, S. P.; Faure, S.; El Blidi, L.; **Aitken, D. J.** Total Synthesis of Cyclotheonamide C by Use of an α-Keto Cyanophosphorane Methodology for Peptide Assembly. *Eur. J. Org. Chem.* 2008, *30*, 5067–5078.

36. Nicolaou, K. C.; Majumder, U.; Roche, S. P.; **Chen, D. Y.-K.** Construction of the "Left Domain" of Haplophytine. *Angew. Chem. Int. Ed.* **2007**, *46*, 4715–4718. PMID: 17559182

37. Aitken, D. J.; Faure, S.; Roche, S. Synthetic approaches to the Southern Part of Cyclotheonamide C. *Tetrahedron Lett.* **2003**, *44*, 8827–8830.

Selected Poster Presentations at National & International Meetings:

1. "A Novel N-Alkoxy-α-Amino Acid Building Block for Peptoid Synthesis" Richaud, A. D.; Roche, S. P.. Poster presented at the *11st Annual World Protein & Peptide Conference (PepCon)*, March **2018**, Miami, Fl, **USA**.

2. "Study of regioselective House–Meinwald Rearrangement (HMR) of spiro-epoxides" Jeedimalla, N.; Roche, S. P. Poster presented at The 18th Florida Heterocyclic and Synthetic Conference (FloHet-2018), March **2018**, University of Florida, Gainesville, Fl, **USA**.

3. "Asymmetric House-Meinwald rearrangement of spiro-epoxide: A unified biomimetic approach to liphagal and frondosin analogues" Jeedimalla, N.; Roche, S. P. Poster presented at the *21st International Conference on Organic Synthesis (ICOS)*, December **2016**, IIT Bombay, **India**.

4. "Revisiting a photochemical, biomimetic hemisynthesis strategy towards bielschowskysin" Scesa, P.; West, L. M.; Roche, S. P. Poster presented at the *21st International Conference on Organic Synthesis (ICOS)*, December **2016**, IIT Bombay, **India**.

5. "Integration of a novel Green Chemistry experiment, using a visible light photocatalyst, into the Organic Chemistry lab at Florida Atlantic University " Beckwith, D.; Roche, S. P.; Rezler, E. M. Poster presented at the *245th American Chemical Society National Conference*, April **2013**, New Orleans, LA, **USA**.

INVITED PROFESSIONAL TALKS

02/2022	GRC Chemistry and Biology of peptides; Postponed
12/2021	PacifiChem; Virtual
09/2019	UT San Antonio
09/2019	Baylor University
04/2019	Brandeis University
03/2018	PepCon 2018 (@ University of Miami)
03/2018	FloHet 2018 (@ Univeristy of Florida)
11/2016	Northeastern University
11/2016	Boston College
11/2016	Boston University
12/2015	PacifiChem 2015; Hawaii
08/2009	238th ACS meeting; Washington D.C.
03/2008	UK-Singapore symposium; Singapore
09/2007	@-STAR-Noyori Ist symposium; Singapore

RESEARCH GRANTS

Pending Research Support:

Florida Health Department—Bankhead-Coley— Roche (Role: **PI**) 05/2022 – 04/2025
"Chemical and Biological Studies of Small-molecule Inhibitors of the PD-1:PD-L1 Checkpoint"
The goal of this project is to discover small-molecule inhibitors of protein-protein interactions (PPIs) and specifically the PD-1/PD-L1 checkpoint in cancer immunotherapy (hepatoma, melanoma resistant to both BRAF and MEK inhibitors, and NSCLC resistant to cisplatin).
Direct cost: $ 782,464 (TOTAL AWARD: $ 889,084)

NIH-NIGMS RO3 Roche (Role: **PI**) 07/2022 – 06/2024
"Rational Design of Covalent Inhibitors of the PD1/PD-L1 Checkpoint."
Our proposal outlines a strategy that combines the synthesis of long *β*-hairpins closely mimicking the native fold of antibody loops while integrating electrophilic warheads for covalent binding to the target PD-1 protein.
Direct cost: $ 100,000 (TOTAL AWARD: $ 145,325) IMPACT SCORE 32

Current Research Support:

1R21GM132754-01 Roche (Role: **PI**) 08/2019 – 04/2022
"*Flexible Rigidity in Peptide Drug Design for Protein-Protein Interaction Inhibitors*" link
The goals of this project are to a) decipher potential paratopes of FDA-approved monoclonal antibodies and b) to develop a novel technology for the synthesis of flexible hairpins that will mimic these paratopes of interest into small-molecule hairpins to explore a novel chemical space in peptide drugs.
Direct cost: $ 275,000 (TOTAL AWARD: $ 398,825) 4TH PERCENTILE

Completed Research Support:

1R15 GM116025-01 Roche (Role: **PI**) 09/2016 – 12/2019
"*Asymmetric Synthesis of Unnatural α-Amino Acids: Applications to Natural Products*" link
This grant focused on undergraduate student training and research experience in peptide chemistry. The project entails the development of a novel synthetic strategy for the asymmetric synthesis of non-proteinogenic α-amino acids and some uniquely challenging α,α-disubstitutted α-amino acids embedded in natural products.
Direct cost: $ 292,000 (TOTAL AWARD: $ 432,869)

MITACS Fellowship Roche (Role: **PI**) 05/2019 – 08/2019
"Synthesis of Small-molecule β-Hairpin Inhibitors of the PD-1:PD-L1 Checkpoint"
Internship in partnership with Universities in Canada. The Goal of the project was to develop the synthetic and analytical skills of the student and to address the question of peptide folding through diverse NMR experiments and denaturation studies by circular dichroism spectroscopy.
Total Fellowship award: $ 6,000

FAU-Technology Grant Roche (Role: **PI**) 2017-2018
"*Acquisition of an NMR-400 MHz to Foster the Next Generation of Skilled STEM Students from FAU*"
This proposal was awarded for the active involvement of undergraduate students in research (Independent research CHM 4905) and strengthen the NMR core facility at FAU.
Direct cost: $ 147,800 (TOTAL AWARD: $ 195,000)

PROFESSIONAL ACTIVITIES

Created and launched the FAU-SCRIPPS internship program, 2015 – Present

Established an internship program with the top-5% ranked engineering schools (France) 2012 – Present

Seminar Coordinator at FAU, Department of Chemistry and Biochemistry "*ChemImpact Series*", 2013 – 2015

Eli Lilly collaborator; Our compound library proposal was selected for the Automated Laboratory Synthesis (ASL) High Throughput Screening Facility OIDD program (2016-18)

Manuscript Reviewer

Nature Scientific Report
Eur. J. Org. Chem.
Eur. J. Med. Chem.
J. Am. chem. Soc.
Org. Lett.
Adv. Synth. Cat.
Tetrahedron Lett.
J. Org. Chem.
Beilstein J. Org. Chem.
Molecules

Proposal Reviewer

National Institute of Health (3 proposals–2016)
National Institute of Health (ad-hoc panelist–2021)
GRIP Grants at FAU (3 proposals-2015)
SURF Grants at FAU (6 proposals-2015-2018)

Editorial Board Member

Organics (New Open Access Journal from MDPI 2020–) ISSN 2673-401X Link
Guest Editor for a Special Issue "*Pericyclic Reactions in Organic Synthesis*" Link

Symposium Chair Organizer---Organic Chemistry Division (2020–2021)

American Chemical Society 96th Florida Annual Meeting and Exposition (FAME) conference, Link

TEACHING EXPERIENCE at FAU

Undergraduate Courses

- CHM 2210 - Organic Chemistry I (Taught 8 semesters, over 2,300 students)
- CHM 2210 – Organic-I Discussion/Bonding (Taught 3 semesters, over 500 students)
- CHM 4220 - Organic Chemistry III (Taught 3 semesters, 30 students)

Graduate Courses

- CHM 6225 - Advanced Organic Chemistry (*New course developed*, taught 2 semesters, 15 students)
- CHM 6157 – Instrumentation (Taught 2 semesters, 35 students)
- CHM 6380 – Topics in Stereochemistry (*New course developed*, taught 3 semesters, 18 students)

STUDENTS PLACEMENT

Our research group has an excellent placement record for group members. Past postdoctoral fellows and undergraduate students hold academic and industrial positions:

Postdoctoral Fellows:

- Dr. Jean-Jacque Youte Tendoung (***6 months at FAU:*** funder and CEO of a start-up company in France StrainChem for custom synthesis (http://www.strainchem.com/))
- Dr. Bret Tréguier (***2 years at FAU***: Lecturer in France (CNRS, Maître de conférence, Université de Rouen)
- Dr. Koushik Goswami (***9 months at FAU***: Lecturer at the Indian Institute of Technology (IIT) Kharagpur)
- Dr. Gregory Boyce (***9 months at FAU:*** Assistant Professor of Chemistry at Florida Gulf Coast University)
- Dr. Mehdi Zaghouani (***2 years at FAU***: Research Scientist position in France (2019, Université d'Orléans)
- Dr. Guangkuan Zhao (***2 years at FAU***: Second postdoctoral position in China 2022-)

Graduate Students: *(5 Graduate students; 2 students graduated from the group by 07/2019)*

- **1- Dr. Shyam Samanta *Graduated*** with a PhD, and joined the Bannister Group at the SCRIPPS Florida. (4 publications and 1 manuscript in preparation)
- **2- Dr. Nagalakshmi Jeedimalla *Graduated*** with a PhD, and joined the industry at API Pharma Tech as a Research Chemist level 2.
- **3- Alexis Richaud (GS5):** PhD student joined my group in the Fall 2017; Alexis is currently working on the synthesis of non-proteinogenic α-amino acids and some peptoids foldamers for the synthesis of β-hairpins.
- **4- Sarah Naylon (GS2):** MS student joined my group in the Fall 2020; Sarah is currently working on the synthesis of β-hairpin covalent inhibitors targeting lysine residues in proteins.

- **5- Hunter Gaenz (GS1):** PhD student joined my group in the Fall 2021; Hunter is currently working on the synthesis of natural products to explore various synthetic strategies of dearomatization.

Graduate Students in rotation only:

- **6- Krishna Yadavalli:** 1 year 2013-2014 and transitioned to the Lepore group at FAU.
- **7- Tanya Kelly:** 1 year 2013-2014 before moving to SCRIPPS Florida and UM.
- **8- Miran Mavlan:** 1 semester Fall 2014 before moving to Purdue University.
- **9- Yong Fan:** 1 semester Fall 2015. Mr. Fan moved back to China.
- **10- Thomas Kempton:** 2 semesters Fall-Spring 2018/19. Mr. Kempton was hired by a local company working on electrochemistry Dioxide Materials.

UG Students: *(>30 UG students total; 2 UG are currently working in the lab)*

Student highlights:

- *2 Current members*: Spring 2021-; Jillene Moxam, and Adrian Romoff.
- Ms. Jillene Moxam (FAU-UG grant awarded 2021), ***accepted*****:** MS in Social Medicine at Columbia University
- Mr. Daniel Garcia (FAU-UG grant awarded 2018), ***position*****:** PhD in Chemistry at the University of Pittsburgh
- Mr. Charles Shearer (9 semesters, Honors program; FAU-UG grant awarded 2016, 2017, 2018, and SURF grant 2017), ***position*****:** MD/PhD at Georgetown University. Take a look at Charles' project: *Link*
- Ms. Aya Tal-mason (3 semesters 2016) (FAU-UG grant 2016), ***position*****:** MS in Biomedical Research at UF.
- Mr. Stephen Zorc (Honors program: 4 semesters 2014-15; FAU-UG grant awarded 2015), ***position*****:** MD-PhD program at the SCRIPPS Florida (Fall 2018-present).
- Mr. Aleem Khan (2 semesters 2014), ***position*****:** MD-PhD program at Boston University (Fall 2015-present).
- Ms. Madison Flint (6 semesters 2011-13; FAU-UG grant awarded 2012), ***position*****:** PhD at UF 2014-2020, awarded with a graduate school fellowship affording her a full salary for 4 years of research assistantship.
- Ms. Jennifer Johns (2 semesters 2012-2013), ***position:*** formulation chemist position at GoodCat Laboratories (Florida).
- Ms. Rhonda Penn (2 semesters 2011-12), ***position***: analytical chemist (Fibertec Inc., Michigan).

International Students: 14 students in 9 years for the Summer Research Training Program (5 months)

- 13 students from France in their second year of engineering school (BS/MS-level) for summer internship at FAU. Emmanuelle Réaux, Camille Jacquet, Marine Gosselin and Gwendoline Lebrun (ENSCCF; **2012-13** & **2015**); Laurine Guillaume (ENSCMu; **2014**); Benjamin Manga, Bastien Buissiere, Diana Bahneva, Baptiste Aumond, Oriane Desaunay, Jessica Michielleto, Samir Hobloss, and Linda Bui (ENSCP ChimieParisTech; **2014-2021**). As shown in the list of publications, five students from this internship pipeline already published their internship work.
- Summer **2019**: Laura Viala on a MITACS fellowship from Canada, University of Quebec.

SERVICE and PROFESSIONAL DEVELOPMENT

2017-18 (Community Outreach for National Chemistry Week): *Link* Our group presented some simple experiments to introduce Organic Chemistry to elementary school students. We used a thematic around the simple building blocks of life (*e.g.* H_2O, CO_2, O_2) to discover the structure of molecules such as natural products from food, essential oil fragrances, and more complex proteins.

Member Website Committee: 2012–2013

Member Graduate Admissions Committee: 2013–present

Member Instrumentation Committee: 2015 – present

Member Strategic Planning Committee, College of Science: 2017–2018

Member Dean of the College Search Committee, College of Science: 2021–2022

Thesis and Dissertation Committees:

At FAU

- Mr. Mohammed Alhuniti (Lepore Group, PhD) defended PhD thesis in 2015
- Mr. Yingzang He (West Group, PhD) defended PhD thesis in 2015
- Mr. Andrew Hall (West Group, PhD) defended PhD thesis in 2016
- Mr. Elijah St Germain (Lepore Group, PhD) defended PhD thesis in 2017
- Mr. Paul Scesa (West Group, PhD) defended PhD thesis in 2020
- Mr. Timothy Foo (Terentis Group, PhD) defended PhD thesis in 2021
- Mr. Johnathon Simpson (West Group, MS) defended MS thesis in 2021
- Ms. Jennifer Luchs (Du group, PhD) (in progress)
- Mr. Silas Hintze (Lepore Group, PhD) (in progress)

At the SCRIPPS Florida

- Mr. John Whitaker (Roush Group; SCRIPPS) defended PhD thesis in 2012
- Mr. Maben Ying (Roush Group; SCRIPPS) defended PhD thesis in 2015
- Ms. Xiang "Alison" Gao (Snyder Group; SCRIPPS) PhD thesis defense in 2017

RESEARCH ACTIVITIES in a NUGGET

The PI, Stéphane Roche, was promoted to the rank of tenured Associate Professor at FAU in the fall of 2018. Our program is focused on the discovery of new and practical synthetic methodologies with broad substrate scope, chemo- and stereoselectivity to access intricate natural products and some other medicinally relevant molecules. We seek to accomplish the most efficient construction of these molecular architectures, through the design of innovative chemical strategies often inspired by some biosynthetic pathways (biomimetic transformations). This provides us with the ability to readily synthesize small-molecule analogs to study the molecular features responsible for a phenotypic response in a given biological assay. Terpenes and complex peptides are the main classes of compounds that constitute the platform for our research. We are actively engaged in several collaborative projects with academic colleagues to evaluate our compound collections against various diseases: *hypercholesterolemia* (PCSK9 inhibitors with Dr. J. Liu @ VA Palo Alto), tubulin polymerization inhibitors and PD-1:PD-L1 inhibitors for *leukemia and lung cancers* (Prof. Minond @ Auburn University, and MD/researcher N. Savaraj @ University of Miami Medical School), and PDF inhibitors: *bacterial infections* (Prof. Huigens III @ University of Florida) and Dr. W. Wintermeyer (@ Max Planck Institute for Biophysical Chemistry in Göttingen) who is testing our synthetic peptides on protein synthesis targets. We are also actively collaborating with Dr. M. Feig for the computational modeling of hairpin folds (Michigan State University) and with Dr. G. Gutierrez expert in protein•drug complex co-crystallization and X-Ray analysis (Indiana University at Bloomington).

Past and Present Collaborators

Dr. E. N. Jacobsen, Chemist @ Harvard University. Longtime collaborator (10 years); engaged in the asymmetric synthesis of non-proteinogenic α-amino acids.

Dr. N. Savaraj, MD, Researcher and PI @ VA Miami and UM Medical Center. Longtime collaborator and co-PI (5 years); engaged in the biological evaluation of several antitumoral chemotypes prepared by our group.

Dr. M. Feig, Michigan State University. Engaged in computational studies on the stabilization of bulged hairpins found in antibodies. (2019-present)

Dr. R. Huigsen III, Medicinal chemist@ University of Florida, College of Pharmacy. Examined the antibacterial activity of a series of fumimycin analogues (peptide deformylase inhibitors) synthesized in our lab.

Dr. W. Wintermeyer, Biologist, Protein synthesis @ Max Planck Institute, University of Göttingen, Germany. Examined the bacterial activity and protein synthesis inhibition induced by a series of fumimycin analogues.

Dr. G. Gonzales-Gutierrez, specialist of protein X-ray @ Indiana University Bloomington. Engaged in crystallographic studies of the PD-1 hairpin inhibitors synthesized in our lab.

Dr. J. Inglese, Director of NIH center @ NCATS. Evaluated azapodophyllotoxin analogues by HTS on different model diseases. (2014-present)

Dr. J. Liu, Principal Investigator at the Research & Development Service; VA Palo Alto. Evaluated potential PCSK9 inhibitors (2016-2017)

Eli Lilly (High Throughput Screening Facility) OIDD program and ASL program (2016-18)

Scientific Contributions

Natural product synthesis. One foci of my research program at FAU focuses on probing the biosynthetic pathways of a number of diterpene natural products by developing the appropriate biomimetic transformations to streamline the construction of these complex polycyclic natural products. In collaboration with the West lab, we reported the hemisynthesis of briareolate ester B, providencin, and the bielschowskysin skeleton. In these projects, we uncovered several photo-catalyzed transformations (oxa-6π electrocyclization, transannular [2+2] photocycloaddition) as well as a practical stereoselective dearomatization strategy of furans. ***Significance***: From a fundamental stand-point, the total synthesis of natural products remains one of the most exhilarating areas of chemical research by providing a unique platform for the discovery of novel technologies, methodologies and synthetic strategies to provide a more sustainable and reliable access to biologically active molecules. Our methodologies have a profound impact on the synthetic planning of complex natural products with atom-, step-, and redox-economy which enabled us to prepare series of bioactive analogues and discover an active epoxide chemotype against a KRAS mutant NSCLC cell line. ***Contribution:*** The PI (Roche) created the project and set-up a collaboration with Lyndon West (FAU) to isolate the proposed biogenetic precursors of complex diterpene natural products and to explore the potential of regioselective transformations within these macrocycles.

a. Hall, A.; **Roche, S. P.; West, L.** Synthesis of Briarane Diterpenoids: Biomimetic Transannular Oxa-6π Electrocyclization Induced by a UVA/UVC Photoswitch. *Org. Lett.* **2017**, *19*, 576–579. PMID: 28080074

b. Scesa, P.; Wangpaichitr, M.; Savaraj, N.; **West, L.**; **Roche, S. P.** A Kinetic Dearomatization Strategy for an Expedient Route to Bielschowskysin Skeleton. *Angew. Chem. Int. Ed.* **2018**, *57*, 1316–1321. ***Selected Hot Paper***. PMID: 29232501

c. **Roche, S. P.** Recent Advances in Oxa-6π Electrocyclization Reactivity for the Synthesis of Privileged Natural Product Scaffolds. *Organics* **2021**, *2*, 376–387. *Link*

d. Scesa, P.; **West, L. M.**; **Roche, S. P.** Role of Macrocyclic Conformational Steering in a Kinetic Route toward Bielschowskysin. *J. Am. Chem. Soc.* **2021**, *143*, 7566–7577

Platform for the asymmetric synthesis of non-proteinogenic amino acids*:* Another direction of my research program seeks to develop a practical and asymmetric synthetic approach to various classes of non-proteinogenic α-amino acids. We recently reported a high yielding one-step synthesis of α-haloglycine esters and the direct one-pot functionalization of these building blocks into α-arylated amino acids. In collaboration with the Jacobsen group (Harvard University), we exploited the unique reactivity of these building blocks as iminium surrogates to advance both asymmetric Mannich and Friedel–Crafts routes to enantioenriched α-amino esters. ***Significance***: Using the concept of anion-binding catalysis promoted by chiral thioureas, halogen abstraction from α-haloglycine ester and other amino acid precursors can be exploited to form several types of C–C bond highly stereoselectively and synthesize numerous classes of unnatural α-amino acids in a highly enantioselective fashion. ***Contribution:*** The PI (Roche) created the project in collaboration with Eric Jacobsen to examine several aspects of the underexplored chemistry of α-haloglycine esters.

a. **Roche*, S. P.**; Samanta, S. S.; Gosselin, M. M. J. Autocatalytic One Pot Orchestration for the Synthesis of α-Arylated α-Amino Esters**.** *Chem. Commun.* **2014**, *50*, 2632–2634. PMID: 24471165

b. Wasa, M.; Liu, R. Y.; **Roche*, S. P.**; **Jacobsen*, E. N.** Asymmetric Mannich Synthesis of α-Amino Esters by Anion-Binding Catalysis. *J. Am. Chem. Soc.* **2014**, *136*, 12872–12875. PMID: 25178040

c. Samanta, S. S.; **Roche, S. P.** Synthesis and Reactivity of α-Haloglycine Esters: Hyperconjugation in Action. *Eur. J. Org. Chem.* **2019**, 6597–6605. ***Editor Choice Issue Cover:*** *Link* PMID: 32351314

d. Bendelsmith, A. J. ; Kim, S. C. ; Wasa, M.; **Roche, S. P.**; **Jacobsen*, E. N.** Enantioselective Synthesis of α-Allyl Amino Esters via Hydrogen-Bond Donor Catalysis*. J. Am. Chem. Soc.* **2019**, *141*, 11414–11419. PMID: 31280564

e. **Roche, S. P.** In the pursuit of (ald)imine surrogates for the direct asymmetric synthesis of non-proteinogenic α-amino acids. *Synthesis* **2021,** *53*, 2767–2776.

Proteomimetics: Access to β-hairpins with long loops. In this more recent project, we are poised to study a class of β-hairpin peptides harboring long non-canonical loops as to advance a novel chemical and conformational space of effective protein–protein interaction (PPI) inhibitors (500-800 $Å^2$ for 1.5-3 KDa). The underlying idea of our strategy is to miniaturize the CDR-H3 loops found in biologically active antibodies into β-hairpin scaffolds that will mimic closely their native fold. To this aim, we advanced a synthetic technology named β-straps (*str*and+c*ap*) which enable the folding of hairpins with long loops (>10 residues) of variable plasticity. To further improve this biomimetic approach, we are currently introducing a flexible hinge motif in between the stack and loop sequences of hairpins which should allow some plasticity for cell permeability and ultimately create an alternative strategy to macrocyclic and other stapled peptides for studying novel classes of PPI inhibitors. ***Significance***: Overall, our approach will improve the synthetic access to loops of conceptually any sequence, length, and conformational strain to develop β-hairpins of high affinity to their biological target and rapidly evaluate the potential introduction of electrophilic warheads within the scaffolds to enhance the potency of the designed PPI inhibitors.

a. Richaud, A. D.; **Roche, S. P.** Structure–Property Relationship Study of N-(Hydroxy)Peptides for the Design of Self-Assembled Parallel β-Sheets. *J. Org. Chem.* **2020**, *19*, 12329–12342.

b. Richaud, A. D.; Zhao, G.; Hobloss, S.; **Roche, S. P**. Folding in Place: Design of β-Strap Motifs to Stabilize the Folding of Hairpins with Long Loops. *J. Org. Chem.* **2021**, *86*, 13535–13547.

c. Zaghouani, M.; Zhao, G.; Richaud, A. D.; Wangpaichitr, M.; Savaraj, N.; **Roche, S. P.** Bent to Bind: Exploiting the Programmed Death-1 Immunoreceptor Plasticity to Design β-Hairpin Inhibitors Mimics of Pembrolizumab. *ChemBioChem* **2022** (*manuscript under review*).