Generalità de candidato. Michele Fiore, Nato a vallo della Lucania (SA) il 19/12/1977, cittadino italiano, residente a Villeurbanne, Francia, Rhone Alpes; iscritto alle liste AIRE dal 2012 presso il comune di Arpaia (BN, Italia) e il consolato di'Italia a Lione (Francia).

Contatti del candidato. Email di contatto principale, presente anche sul sito PICA/login MIUR= <a href="michele.fiore.chimico@gmail.com">michele.fiore.chimico@gmail.com</a>; altri contatti: <a href="michele.fiore@univ-lyon1.fr">michele.fiore@univ-lyon1.fr</a>; prof.michele.fiore@gmail.com

Contatto telefonico: 351 986 2237; +33 (0)7 81 71 13 22

Informazioni aggiuntive

Orcid ID: 0000-0001-8176-9249; Scopus Author ID: 57201759668

URL: http://www.icbms.fr/co2glyco/effectif/fiore

#### Titoli accademici.

2019: *Habilitation à Diriger les Recherches* obtained at the l'Université Claude Bernard Lyon Titolo: "Prebiotic synthesis of phospholipids and membranogenic compounds: use and application in systems chemistry"; Jury: Prof. Philippe Barthélémy, Dr. Carole Chaix-Bauvais, Dr. Sabine Chierici, Prof. Agnès Girard-Egrot, Prof. Julien Leclaire (president), <u>Dr. Robert Pascal (rapporteur)</u>, Prof. Florence Popowycz, Prof. Pierre Strazewski, <u>Prof. Yannick Vallée (rapporteur</u>)

2003 - 2007	Ph.D. in Agrochemistry and Agrobiology		
	Faculty of Agronomy, Department of Plant, Soil, Animal and Environmental		
	Science, University of Naples "Federico II"/ Italy, Ph.D. supervisor: Prof.		
	Antonio Evidente		
2001 - 2002	Master in Organic Chemistry		
	Faculty of applied Science, Department of Chemistry, University of Naples		
	"Federico II"/ Italy, Supervisor, Dr. Falvio Cermola		

### Formazione (periodi all'estero di formazione a carattere scientifico)

2023/2024	Long mission*	Chemistry Department	University of Siena, Italy; University of Salerno, Italy;
2016	Short mission <sup>§</sup>	Chemistry Department	University "Aldo Moro" – Bari, Italy

2014	Short	FLinT-Fundamental Living	University	of	sud
	mission §	Technology	Danemark (S	DU) - O	dense,
			Danemark		

\*CRCT Université de Lyon Claude Bernard Lyon 1 (Changement des Recherches – Changement des Thématiques) §Short Term Scientific Mission (STSM), COST Action CM1304;

2013	Short	Organic Chemistry	University of Bristol –
	mission †	Department	Bristol,
		·	Royaume-Uni

<sup>&</sup>lt;sup>†</sup> Short Term Scientific Mission (STSM), COST Action CM1102

2005	PhD	Chemistry and Biochemistry	University of Oxford -
	program <sup>‡</sup>	Department	Mississippi
			(OLEMISS) United States

<sup>&</sup>lt;sup>‡</sup>USDA, ARS, NPURU (*United States Departement of Agriculture, Agricultural Research Service, Natural Product Utilisation Research Unit*) dans le programme italo-américain d'échange d'étudiants

### Possesso del requisito ASN (Abilitazione scientidica Nazionale)

17/01/2020 Abilitazione Scientifica Nazionale alle funzioni di professore universitario di seconda fascia nel Settore Concorsuale 03/C1 - CHIMICA ORGANICA, validià 10 anni (scadenza, 30 gennaio 2030)

#### Altre Abilitazioni.

Inscription sur la liste de qualification aux fonctions de Professeur des Universités obtenu le 06/02/2020 N° 20132343054 pour la section 32 (corrispondente alla abilitazione alla fascia I, settore concorsuale 03/C1 – Chimica Organica)

#### **Working experiences**

2014 – present *Maitre de conference,* HDR (**Associate Professor,** Organic Chemistry)
Faculty of Science/ Department: *Institut de Chimie et Biochimie Moléculaires et Supramoléculaires,* University of Lyon, Claude Bernard Lyon 1/ France

## Post-doctoral working experiences

- 2014 2014 Research Director (Directeur de recherche), CDD (Vaccine development)

  Faculty of Science, Department of Molecular Chemistry, University of Grenoble Rhone Alpes/ France
- 2012 2014 **Post-doc** (Organic Chemistry, Vaccine development)

  Faculty of Science, Department of Molecular Chemistry, University of Grenoble Rhone Alpes/ France
- 2011 2012 **Post-doc** (Organic Chemistry, Vaccine development)

Faculty of Science, Department of Molecular Chemistry, University of Grenoble Rhone Alpes/ France

2009 – 2011 Scientist (Medicinal Chemistry)

Siena Biotech SPA, Department of Medicinal Chemistry, Siena/ Italy

2007 – 2009 **Post-doc** (Organic Chemistry)

Faculty of Science/ Department of Chemistry, University of Ferrara/ Italy

- Attività di ricerca
- Organizzazione, direzione e coordinamento di centri e/o gruppi di ricerca nazionali:
- 1. Organizzazione, direzione e coordinamento; 2023/2024 CRCT (Changement de Recherche/Changement Tematique). Two semesters were obtained for researching organic chemistry, synthetic biology, and bioactive compounds developments guest of Prof. Federico Rossi/Prof. Jack Chan at the Laboratorio di chimica Università di Siena, Italy; Research activities: Synthesis and characterization of phospholipid analogs for understanding the emergence of homochirality in the origin of life studies. Faculty of Science, ICBMS, University of Lyon, Claude Bernard Lyon 1.
- **2.** Organizzazione, direzione e coordinamento; **2023** Submitted. REAL-P project in collaboration with Prof. Marco Terreni at the University of Pavia, Faculty of Pharmacy Proposed research activity: preparation of giant unilamellar and large unilamellar vesicles made of phospholipid analogs as vaccine carriers/drug delivery systems against glioblastoma and other neurodegenerative diseases. Faculty of Science, ICBMS, University of Lyon, Claude Bernard Lyon 1.
- 3. Organizzazione e coordinamento; 2012 2014 Research project in collaboration with the research group of Prof. Cristina Nativi, University of Florence on the synthesis, chemical and biological characterization of full synthetic vaccines against melanoma Faculty of Science/ Department of Molecular Chemistry, University of Grenoble Rhone Alpes in the frame of the research project financed by the national league against cancer grant n° JG/IQ 3194 Faculty of Science/ Department of Molecular Chemistry, University of Grenoble Rhone Alpes/ France; Fellowship of the Ligue Nationale Française Contre le Cancer
- Organizzazione, direzione e coordinamento di centri e/o gruppi di ricerca internazionali:
- 1. Partecipazione e coordinamento MSCA COFUND International Doctoral Programme HORIZON-MSCA-2022-COFUND-01 no. 101126656

ArchiFun: Architecture, function and dynamics in Life Sciences

Beneficiary: Université Claude Bernard Lyon 1

**2. Direzione, organizzazione e coordinamento di** di un progetto di ricerca sottomesso alla call ANR (Agence Nationale de Recherche, Agenzia Nazionale della Ricerca) di 500k in collaborazione con

i gruppi di ricerca dei professori Guillaume Pilet (LMI, UCBL Lyon 1), Saida Mabarek (ICBMS, UCBL, Lyon 1), Federico Rossi (University of Siena, Italy) Nel caso di accettazione del progetto, il finanziamento sarà attribuito e spendibile presso i dipartimenti di appartenenza dove il sottoscritto potrà svolgere attività di ricerca coordinando un team di 2 ricercatori non strutturati (1 dottorando/a, 1 personale tecnico) e 2 strutturati per una durata complessiva di 36 mesi.

- **3. Partecipazione :** DÉVELOPPEMENT D'UN BIOMÉDICAMENT ANTI-OBÉSITÉ, INHIBITEUR DES LIPASES DIGESTIVES, finanziato dal comitato misto Franco-Tunisino. Code Campus France 50314TG, Code CMCU 24G0801 Il mio ruolo é la caratterizazzione chimica di sostanze naturali che saranno poi testati quali inibitori di lipasi.
- **4.** Organizzazione, co-direzione e coordinamento ; 2017 2022 Volkswagen Siftlung "LIFE? A FRESH APPROACH TO THE ORIGINS OF LIFE" grant AZ92850, Faculty of Science, ICBMS, University of Lyon, Claude Bernard Lyon 1.
- **5.** Organizzazione, direzione e coordinamento; 2023 2026 Research project "Lyso Probes", Faculty of Science, ICBMS, University of Lyon, Claude Bernard Lyon 1. Direzione di un/a dottorando/a di ricerca.
- **6.** Organizzazione, direzione e coordinamento; 2012 2014 Research project for the French Ligue against cancer grant n° JG/IQ 3194 Faculty of Science/ Department of Molecular Chemistry, University of Grenoble Rhone Alpes/ France; Fellowship of the Ligue Nationale Française Contre le Cancer

### o Partecipazione a centri e/o gruppi di ricerca nazionali:

**1. 2023 CRCT** (Changement de Recherche/Changement Tematique). Two semesters were obtained for researching organic chemistry, synthetic biology, and bioactive compounds developments. Prof. Federico Rossi/Prof. Jack Chan, Laboratorio di chimica Università di Siena, Italy)

Research activities: Synthesis and characterization of phospholipid analogs for understanding the emergence of homochirality in the origin of life studies.

- 2. Organizzazione, co-direzione e coordinamento; 2017 2022 Volkswagen Siftlung "LIFE? A FRESH APPROACH TO THE ORIGINS OF LIFE" grant AZ92850, Faculty of Science, ICBMS, University of Lyon, Claude Bernard Lyon 1.
- 3. Organizzazione, direzione e coordinamento; 2023 2026 Research project "Lyso Probes", Faculty of Science, ICBMS, University of Lyon, Claude Bernard Lyon 1.
- **4.** Organizzazione, direzione e coordinamento; **2012 2014** Research project for the French Ligue against cancer grant n° JG/IQ 3194 Faculty of Science/ Department of Molecular Chemistry, University of Grenoble Rhone Alpes/ France; Fellowship of the Ligue Nationale Française Contre le Cancer
- o Direzione di comitati editoriali di riviste:

2022. Guest Editor for the Special Issue of LIFE (ISSN 2075-1729) in the series Origin of Life: "The Origin and Early Evolution of Life: Prebiotic Systems Chemistry Perspective"

https://www.mdpi.com/journal/life/special issues/Prebiotic Systems Chemistry Biom olecules

2019. Guest Eidtor for the Special Issue of LIFE (ISSN 2075-1729) in the series Origin of Life: "The Origin and Early Evolution of Life: Prebiotic Chemistry of Biomolecules" <a href="https://www.mdpi.com/journal/life/special">https://www.mdpi.com/journal/life/special</a> issues/Prebiotic Chemistry

### o Partecipazione a comitati editoriali di riviste:

From 2019 - Member of the editorial board of Life (Basel) ISSN 2075-1729

2022. Guest Editor for the Special Issue of LIFE (ISSN 2075-1729) in the series Origin of Life: "The Origin and Early Evolution of Life: Prebiotic Systems Chemistry Perspective"

https://www.mdpi.com/journal/life/special issues/Prebiotic Systems Chemistry Biom olecules

2019. Guest Editor for the Special Issue of LIFE (ISSN 2075-1729) in the series Origin of Life: "The Origin and Early Evolution of Life: Prebiotic Chemistry of Biomolecules" <a href="https://www.mdpi.com/journal/life/special">https://www.mdpi.com/journal/life/special</a> issues/Prebiotic Chemistry

Prebiotic chemistry and Life's origin

M. Fiore, Editor; Royal Chemical Society, London

(The Chemical Biology series) ISBN: 978-1-78801-749-7 - printed

#### o Conseguimento di premi e riconoscimenti internazionali:

- 2023 Laureate SENS (Soutiens aux Enseignants) for the Project <u>Synthèse</u>, <u>caractérisation et utilisation des Rhodols comme traqueurs lysosomiaux</u>. Acronym: <u>LysoProbes (Synthesis, characterization and use of Rhodols as lysosomal trackers)</u>
- 2. 2023 Laureate CRCT (Changement de Recherche/Changement Tematique). Two semesters were obtained for researching organic chemistry, synthetic biology, and bioactive compounds developments. Prof. Federico Rossi/Prof. Jack Chan, Laboratorio di chimica Università di Siena, Italy)
- 2022 and 2021 Erasmus Grant for teaching activities at University of Milan –
   Bicocca, from the University of Lyon Claude Bernard Lyon 1
- **4.** 2022 1<sup>st</sup> Prize Cozzarelli Award for the following article Altamura et al., *PNAS*, 2021 Vol. 118 No. 7 e2012170118 (author)
- **5.** 2021 and 2022 Editor's choice from *Symmetry* for the following article Altamura et al. *Symmetry* 2020, *12*, 1108; doi:10.3390/sym12071108 (corresponding author)
- **6.** 2020 2023 ; Prime d'Encadrement Doctoral et de Recherche (Grant of 4000 euros each year from 2020 to 2023 ; Premio per la qualità della ricerca)

- **7.** 2017 Volkswagen Siftlung "LIFE? A FRESH APPROACH TO THE ORIGINS OF LIFE" grant AZ92850 (Participant)
- 8. 2014, BQR research project, University of Lyon, Claude Bernard Lyon 1
- 9. 2012 2014, Faculty of Science/ Department of Molecular Chemistry, University of Grenoble Rhone Alpes/ France; Fellowship of the Ligue Nationale Française Contre le Cancer (JG/IQ 3194)

## o Partecipazione in qualità di relatore a congressi e convegni di interesse nazionale:

- 1. Phospholipids and other amphiphilic molecules: Abiotic synthesis and their use in systems chemistry, Salerno, Nov. 2022 (Invited)
- 2. Phospholipids and other amphiphilic molecules organic, evolutionary, and plausible prebiotic synthesis and use in systems chemistry, Naples, Nov. 2018 (Invited)
- 3. Towards the preparation of synthetic outer membrane vesicles (OMVs) As potential vaccines carriers against cancer and infectious diseases, Bari, June 2018 (Invited)
- 4. Phospholipids and other amphiphilic molecules: nature, preparation, and use in systems chemistry, Salerno, Avril 2018 (Invited)
- 5. Multivalent glycocyclopeptides: toward nano-sized glycostructures COST BM1003 Training School Naples, 3rd-5th June 2014, Napoli, Italy (Invited)
- 6. Synthesis of glycopolymers via thiol-ene induced reactions M. Fiore, N. Berthet, O. Renaudet, V. Barbier XIV Convegno-Scuola sulla Chimica dei Carboidrati, Certosa di Pontignano, 22-25 Giugno 2014, Oral comunication
- 7. The synthesis of sugar-based anti-proliferative compounds in neurodegeneratives diseases M. Fiore in behalf of Sienabiotech SPA, XXX Advanced course of Medicinal Chemistry and "E Duranti" National Seminar for PhD Students Urbino July 4-9, 2010
- 8. Synthesis of hetero-glycoclusters as platform for vaccines candidates M. Fiore, B. Thomas, P. Dumy, O. Renaudet XIII Convegno-Scuola sulla Chimica dei Carboidrati, Certosa di Pontignano, 24-27 giugno 2012, Oral communication
- Synthesis of S-glycosyl amino acids via photoinduced thiol-ene coupling S. Pacifico,
   M. Lo Conte, M. Fiore, A. Marra, A. Dondoni XII Convegno-Scuola sulla Chimica dei Carboidrati, Certosa di Pontignano, 20-23 giugno 2010, Oral Comunication
- 10. Photoinduced Thiol Ene Coupling as a Click Ligation tool M. Fiore, A. Marra, A. Dondoni Biotech.Org/ Forte dei Marmi (Lu) 20 23 maggio 2009 (Poster)
- 11. Le fitotossine prodotte da Diplodia corticola associata al deperimento della quercia da sughero in Sardegna" M. Fiore, A. Andolfi, E. Spanu, L. Maddau, A. Franceschini, F. Marras, A. Motta, A. Evidente VII Convegno Nazionale, Giornate di Chimica delle sostanza naturali, 7-10 Giugno 2006, Acquafredda- Maratea Hotel Villa del Mare.
- 12. "LE FITOTOSSINE PRODOTTE DA FUNGHI FITOPATOGENI DELLA QUERCIA DA SUGHERO" A. Andolfi, M. Fiore, L. Maddau, E. Spanu, F. Marras, A. Evidente XXX Convegno Nazionale della divisione di Chimica Organica della Società Chimica Italiana, Siena 19-23 Settembre 2005 (Oral Comunication) (2002 -2003)
- 13. "C-Glicosidi Funzionalizzati Mediante Footossigenazione Sensibilizzata da Coloranti di 2-metossifurani Opportunamente Sostituiti" F. Cermola, M. Fiore, M. R. Iesce, S. Montella. XXVIII Convegno Nazionale della Divisione di Chimica Organica, Roma 16-20 settembre 2002, P-78 (Poster)

14. "Reazioni di [4+2] cicloaddizione di ossigeno singoletto su 2'-(C-glicosil) furani: sintesi di nuovi glucosidi funzionalizzati" F. Cermola, M. Fiore, M. R. Iesce, M. L. Graziano, S. Montella. XI Convegno Nazionale sulle Reazioni Pericicle, Villa Olmo, Como, 15-20 settembre 2003. (Poster)

## o Partecipazione in qualità di relatore a congressi e convegni di interesse internazionale:

- Conference Nationale de Exobiologie Marseille 11-14 octobre 2021 Université Aix-Marseille; Campus de Luminy www.exobiologie.fr/Conference21/ Supported Giant Vesicles as an efficient tool for protocell handling
- 2. Teacher and invited speakerat the international school for PhD RED "Rencontres Exobiologiques pour Doctorants (week 14 Mars 2022) TEICH Parc Onritologique (France)
- 3. Phospholipids and other amphiphilic molecules. Organic, evolutionary and plausible prebiotic synthesis Science of Early Life Conference 2018 June 24 27, 2018, Origins Institute, McMaster University, Hamilton, Canada (Invited)
- 4. Growth and division processes using phospholipid glass-supported vesicles BIONAM 2019 workshop September 29 October 3, 2019 | MSC cruise, Mediterranean Sea
- 5. The phosphorylation of alcohols under plausible prebiotic conditions: a study on the reaction mechanism, Science of Early Life conference, 17-20 November 2019, Conference Center, Kloster Seeon, Bavaria, Germany (Invited)
- 6. Towards Molecular Complexity: At the crossroads between astrophysics and biochemistry. Origin of Life Meeting, Max Plank Institute, Heidelberg, 2-6 May, 2022
- 7. The Use of Chemical Models to Understand the Emergence of Homo-chirality, Prebiotic Systems Chemistry Perspectives, Montpellier, Dec. 2022 (Invited)
- 8. Phospholipids and other amphiphilic molecules: Abiotic synthesis and their use in systems chemistry, Séminaire au sein de l'école doctorale de chimie, Brest, Nov. 2019
- 9. Phospholipids and other amphiphilic molecules organic, evolutionary, plausible prebiotic synthesis and use in Systems Chemistry, Grenoble, Oct. 2019 (Invited)
- Crude Phosphorylation mixtures containing lipid amphiphiles self-assemble to give stable primitive compartments (oral communication) M.Fiore, D. Fayolle, P. Strazweski; Systems Chemistry 2017 Conference (COST action CM1304) 11-15 September 2017, Sopron, Hungary
- 11. Glass Microsphere-Supported Giant Vesicles as Tools for Observation of Self-reproduction of Lipid Boundaries; M. Fiore, O. Maniti, A. Girard-Egrot, P-A Monnard, P. Strazewski (Poster) Systems Chemistry 2017 Conference (COST action CM1304) 11-15 September 2017, Sopron, Hungary
- 12. Rapid purification of giant lipid vesicles by microfiltration. D. Fayolle, M. Fiore, P. Strazweski Meeting of the working group 3 of the COST action CM1304: 30 March 01 April 2017 (not 2016), Warsaw, Poland
- 13. Giant Vesicles (GVs) from naturally swelled mixed and 'incomplete' lipids stability and permeability tests M. Fiore, P-A Monnard, P. Strazewski (Oral comunication)

- Meeting of the working group 3 of the COST action CM1304, Pullach, Parmenides Foundation, Kirchplatz 1, D-82049 Pullach
- 14. Betzabe R, Fiore M, Leveau G, Fayolle D, Strazewski P (2018). Synthesis of an esterified calcein through a Friedel-Crafts-like reaction, by first synthesizing a modified resorcinol through a Mannich reaction, in order to make a membrane impermeable clickable fluorescent probe. In: Conference: 255th National Meeting and Exposition of the American-Chemical-Society (ACS) Nexus of Food, Energy, and Water Location: New Orleans, LA Date: MAR 18-22, 2018 ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY Volume: 255 Meeting Abstract: 1268 Published: MAR 18 2018.
- 15. Synthesis of homo- and hetero-glycoclusters as potential vaccines against cancer M. Fiore, B. Thomas, N Berthet, P. Dumy, O. Renaudet European Young Investigators Workshop "Deciphering the Glycome from synthesis to applications" 17th 20th March 2013 Postdam (Berlin), Germany
- 16. Synthesis of hetero-glycoclusters as new platforms for the construction of anticancer vaccine candidates M. Fiore, B. Thomas, P. Dumy, O. Renaudet 26th INTERNATIONAL CARBOHYDRATE SYMPOSIUM (ICS 2012) Hotel Melià Castilla, 43, Madrid 22 27 July 2012 (FC 169, P 595) (Oral Comunication and Poster)
- 17. Tetravalent GlcNAc Glycoclusters: Influence of the Linker for the Wheat Germ Agglutinin Interaction M. Fiore, N. Berthet, P. Dumy, A. Marra, A. Dondoni, E. Gillon, A. Imberty, O. Renaudet Journée Rhone-Alpes des Biomolécules (JRAB 2012) 01/06/2012 Amphithéatre Ouest de Chimie, Domaine Universtitaire de S. Martin d'Hères, Université de Grenoble, UJF (Poster)
- 18. Conception et Synthese d'hetero-glycoclusters puor l'immunotherapie anticancerouse B. Thomas, M. Fiore, I. Bossu, P. Dumy, O. Renaudet Journée Rhone-Alpes des Biomolécules (JRAB 2011) 27/05/2011 Amphithéâtre de l'ISTIL Université Claude Bernard Lyon1 (Poster)
- 19. "Phytotoxic Metabolites produced by fungi involved in Cork Oak decline" L. Maddau, E. Spanu, A. Franceschini, F. Marras, A. Andolfi, M. Fiore and A. Evidente Proceedings of the 12th Congress of the Mediterranean Phytopatological Union, 11-15 June 2006 Rhodes Island, Hellas
- 20. "Estudio químico y biológico de hongos patógenos de la madera de la vid del género Botryosphaeria" Martos, S.; Evidente, A.; Fiore, M.; Surico, G.; Mugnai, L.; Peduto, F.; Luque, J. XIII Congreso de la Sociedad Española de Fitopatología: pag. 36, Murcia (España) 18-22 september 2006.

#### o Produzione scientifica:

### Articoli in rivista

55 From the RNA-Peptide World: Prebiotic Reaction Conditions Compatible with Lipid Membranes for the Formation of Lipophilic Random Peptides in the Presence of Short Oligonucleotides, and More

Augustin Lopez, Antoine Vauchez, Ghinwa Ajram, Anastasiia Shvetsova, Gabrielle Leveau, **Michele Fiore** and Peter Strazewski

Life **2024**, 14, 108; https://doi.org/10.3390/life14010108

## 54. Synthetic Outer Membrane Vesicles Bearing Tn Antigen

Carolina Chieffo, Arnaud Comte, Peter Strazewski and **Michele Fiore\*** *Eur. J. Org. Chem.* **2023**, e202300820; doi.org/10.1002/ejoc.202300820

## 53. The Origin and Early Evolution of Life: Homochirality Emergence in Prebiotic Environments

Carolina Chieffo, Anastasiia Shvetsova, Fryni Skorda, Augustin Lopez, and **Michele Fiore\*** *Astrobiology*, **2023**, *12*, DOI: 10.1089/ast.2023.0007

**52. Microwave-Assisted Syntheses of Rhodamine, Rhodol, and Fluorescein Derivatives** Carolina Chieffo, Emiliano Altamura, Guillaume Pilet, Saida Mebarek, Peter Strazewski, and **Michele Fiore\*** *ChemPlusChem*, **2023**, *88*, e202300189

## 51. Shedding light on the role of Na, K-ATPase as a phosphatase during matrix vesiclemediated mineralization

Heitor Gobbi Sebinelli, Luiz Henrique da Silva Andrilli, Bruno Zocaratto Favarin, Marcos Antonio Eufrasio Cruz, Maytê Bolean, **Michele Fiore**, <u>Carolina Chieffo</u>, David Magne, Andrea Magrini, Ana Paula Ramos, José Luis Millán, Saida Mebarek, Rene Buchet, Massimo Bottini and Pietro Ciancaglini – *Int. J. Mol. Sci.* **2022**, https://doi.org/10.3390/ijms232315072

# 50. A Comprehensive Characterization of "Off/On" Rhodol-based Lysosomal Tracker for Orthogonal Cellular Analysis by Confocal Imaging

<u>Carolina Chieffo, Emiliano Altamura</u>, Layth Ben Trad, Guillaume Pilet, Ofelia Maniti, Thierry Granjon, Saida Mabarek, Peter Strazewski, **Michele Fiore\*** - *ChemBioChem*, *e202200513*, https://doi.org/10.1002/cbic.202200513

# 49. Chemical Models for Understanding the Emergence of Homo-chirality of Phospholipids for Origin of Life Studies.

<u>Fryni Skorda, Carolina Chieffo</u>, **Michele Fiore\***, *Symmetry*, **2022**, 14, 2109 https://doi.org/10.3390/sym14102109

# **48.** The Origin and Early Evolution of Life: (Prebiotic) Systems Chemistry Perspective Emiliano Altamura, Michele Fiore\*

Life **2022**, 12, 710. https://doi.org/10.3390/life12050710

## 47. Synthesis of Phospholipids Under Plausible Prebiotic Conditions and Analogies with Phospholipid Biochemistry for Origin of Life Studies.

**Michele Fiore\***, <u>Carolina Chieffo, Augustin Lopez, Dimitri Fayolle</u>, Johal Ruiz, Laurent Soulère, Philippe Oger, <u>Emiliano Altamura</u>, Florence Popowycz, and René Buchet

Astrobiology, **2022**, Published Online: 23 Feb 2022 https://doi-org.docelec.univ-lyon1.fr/10.1089/ast.2021.0059 (open access)

### 46. Phosphorylation of prebiotic precursors

<u>Anastasiia Shvetsova</u>, **Michele Fiore**, Peter Strazewski and Isabelle Daniel *Goldschmidt* **2021** *Abstract https://doi.org/10.7185/gold2021.6016* 

## 45. Hydrolysis of Extracellular ATP by Vascular Smooth Muscle Cells Transdifferentiated into Chondrocytes Generates Pi but Not PPi

Rene Buchet, Camille Tribes, Valentine Rouaix, Bastien Doumèche, Michele Fiore, Yuqing Wu, David Magne and Saida Mebarek

Int. J. Mol. Sci. **2021**, 22, 2948. https://doi.org/10.3390/ijms22062948

## 44. Chromatophores Efficiently Promote Light-Driven ATP Synthesis and DNA 3 Transcription Inside Hybrid Multi-Compartment Artificial Cells

E. Altamura, P. Albanese, R. Marotta, F. Milano, M. Fiore, M. Trotta, P. Stano and F. Mavelli *PNAS*, **2021** Vol. 118 No. 7 e2012170118

# 42. Chemical Analysis of Lipid Boundaries after Consecutive Growth and Division of Supported Giant Vesicles

A. Lopez, D. Fayolle, M. Fiore\*, P. Strazewski iScience, 2020, https://doi.org/10.1016/j.isci.2020.101677

## 41. Symmetry Breaking of Phospholipids

M. Fiore,\* R. Buchet,

Symmetry 2020, 12, 1488; doi:10.3390/s

Symmetry **2020**, 12, 1488; doi:10.3390/sym12091488

## 40. Racemic phospholipids for origin of life studies

<u>E. Altamura</u>, A. Comte, <u>A. D'Onofrio, C. Roussillon, D. Fayolle</u>, R. Buchet, F. Mavelli, P. Stano, M. Fiore,\* P. Strazewski

Symmetry 2020, 12, 1108; doi:10.3390/sym12071108

### 39. The Origin and Early Evolution of Life: Prebiotic Chemistry.

#### M. Fiore

*Life*, **2019**, 9, 73; doi:10.3390/life9030073

# 38. Investigating prebiotic protocells for a comprehensive understanding of the origins of life: a prebiotic systems chemistry perspective.

A. Lopez & M. Fiore\*

Life, 2019, 9, 49; doi:10.3390/life9020049

# 37. Towards the preparation of synthetic outer membrane vesicle models with micromolar affinity to wheat germ agglutinin using a dialkyl thioglycoside.

D. Fayolle, B. Doumèche, N. Berthet, O. Renaudet, P. Strazewski, M. Fiore\* Beilstein J. Org. Chem. 2019, 15, 937–946. doi:10.3762/bjoc.15.90

### 36. Identification of a new natural gastric lipase inhibitor from star anise

J. Kamoun, R. Rahiern, M. Sellami, I. Koubaa, P. Mansuelle, R. Lebrun, A. Berlioz-Barbier, M. Fiore, K. Alvarez, A. Abousalham, F. Carrière, A. Aloulou, *Food Funct*, **2019**, *10*, 469-478

## 35. Multivalent Glycomimetics with Affinity and Selectivity toward Fucose-Binding Receptors from Emerging Pathogens

David Goyard, <u>Veronica Baldoneschi</u>, Annabelle Varrot, **Michele Fiore**, Anne Imberty, Barbara Richichi, Olivier Renaudet, Cristina Nativi

Bioconjugate Chemistry 2018, 29 (1), 83-88, DOI: 10.1021/acs.bioconjchem.7b00616

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# **01.** Stimulation of *Orobanche ramosa* seed germination by fusicoccin derivatives: A structure—activity relationship study

Antonio Evidente, Anna Andolfi, Michele Fiore, Angela Boari, Maurizio Vurro

Libri (Autore, Editor)

## 1. Prebiotic chemistry and Life's origin

M. Fiore, Editor; Royal Chemical Society, London

(The Chemical Biology series) ISBN: 978-1-78801-749-7 - printed

## 2. The Origin and Early Evolution of Life: Prebiotic Systems Chemistry perspective (2022)

E. Altamura and M. Fiore, Editors. MDPI, St. Alban-Anlage 66

4052 Basel, Switzerland

ISBN 978-3-0365-4469-4 (Hbk); SBN 978-3-0365-4470-4 (PDF)

## 3. The Origin and Early Evolution of Life: Prebiotic Chemistry (2019)

M. Fiore, Editor. MDPI, St. Alban-Anlage 66

4052 Basel, Switzerland

ISBN 978-3-03921-606-2 (Hbk); ISBN 978-3-03921-607-9 (PDF)

Libri (autore di capitoli)

## 1. Prebiotic Condensing Agents (Chapter 4)

M Fiore\*

In Prebiotic chemistry and Life's origin

M. Fiore, Editor; Royal Chemical Society, London

(The Chemical Biology series) ISBN: 978-1-78801-749-7 - printed

## 2. Prebiotic Amphiphiles: The Systems Chemistry Perspectives (Chapter 9)

M.Fiore\*

In Prebiotic chemistry and Life's origin

M. Fiore, Editor; Royal Chemical Society, London

(The Chemical Biology series) ISBN: 978-1-78801-749-7 – printed

## 3. Abiotic synthesis and role of amphiphiles in the encapsulation process in life's Origin.

Lopez A., Chieffo C., Fiore M.\*

In Prebiotic Chemistry and the Origin of Life (Advances in Astrobiology and Biogeophysics), Editors: Neubeck A. and McMahon, Springer Nature, currently planned publ. Date 21 oct 2021; Springer Nature Switzerland AG Gewerbestrasse 11, 6330; https://doi.org/10.1007/978-3-030-81039-9\_6

## 4. Following the Growth and Division of Lipid Boundaries by Using Glass Microsphere-Supported Protocells (2020)

A. Lopez, C. Chieffo, M. Fiore\*

In: Book Series: Lecture Notes in Bioengineering S. Piotto, S. Concilio, L. Sessa, F. Rossi, Editors Publisher: Springer International Publishing

Print ISBN: 978-3-030-47704-2

### 5. Protecting groups for the primary position of carbohydrates (2018)

M. Donnier-Marechal, S. Vidal, M. Fiore\*

In "Protecting Groups - Strategies and Applications in Carbohydrate Chemistry"

Wiley-VCH, Editor S. Vidal, Université de Lyon, Claude Bernard Lyon 1,

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## 6. Synthetic Vaccines against Cancers (2015)

**M. Fiore**, B. Thomas, G. C. Daskhan and O. Renaudet. In Carbohydrate Chemistry: State of the Art and Challenges for Drug Development, pp. 357-378 (2015) https://doi.org/10.1142/9781783267200\_0014 ISBN: 9781783267194

## 7. Chemical synthesis of carbohydrate-based vaccines against cancer (2013)

M. Fiore, B. Thomas, P. Dumy, O. Renaudet

In Biomaterials for cancer therapeutics, Woodhead Publishing (2013)

DOI: 10.1533/ 9780857096760.2.59; ISBN: 9780857096647

### **Teaching**

2014 – Maitre de conférences, échelon 7, HDR (corresponding to *Professore associato di II fascia, classe V*) Faculté de Science, Institut de Chimie et Biochimie Moléculaires et Supramoléculaires, Université de Lyon, Claude Bernard, Lyon 1 / France, totale des HEQTD = 192

2022 – responsable de l'UE pour le Master 1 "Fonctionnalisation es synthèse organique" CHM1182M

Academic Year	University	Number of hours per year	Décharges / CRCT /
2018 - 2019	Université Claude Bernard Lyon 1	234	
2019 - 2020	Université Claude Bernard Lyon 1	209	
2020 - 2021	Université Claude Bernard Lyon 1	89*	Due to Sars Covid 2019

2021 - 2022	Université Claude Bernard Lyon 1	228		
2022 - 2023	Université Claude Bernard Lyon 1	None	In CRCT (University of Siena, Italy)	

### **Expertise**

- Expert for the scientific evaluation of projects for :

ANR: 2019, 2022, 2023 (Agence Nationale de Recherche, France)

ERC: 2017/2018 (European Research Council)

2017 – 2022 Member of the scientific committee of the Volkswagen Siftlung "LIFE? A FRESH APPROACH TO THE ORIGINS OF LIFE" grant AZ92850 / Germany, France and United States, 2019 – 2022 Member of the scientific committee of Science of Early Life – Kolster Seeon, Germany,

2019 – 2020 Member of the scientific committee of the BIONAM III / Italy

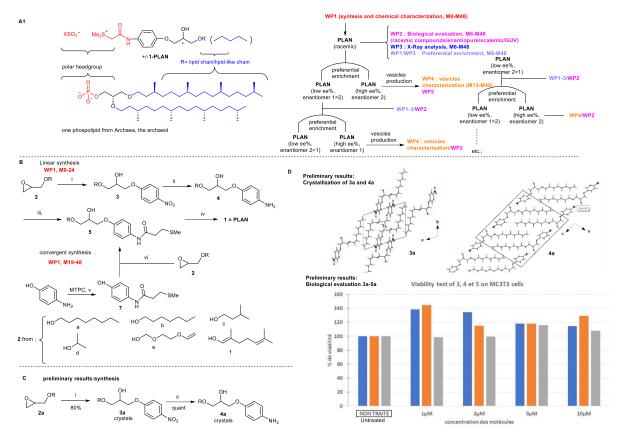
2015 - 2018, Member of the COST action CM1304

2012 – 2014, Member of the COST action CM1102

Research carried out in the frame of the CRCT 2023/2024 at the University of Salerno and Siena.

### Symmetry breaking studies using phospholipid analogs

A series of Phospholipid analogs (PLAN) can be prepared as racemate using two synthetic pathways (convergent and linear), starting from glycidols. Those PLAN show large similarities with Archaea phospholipids, bearing a polar head and a lipidic chain connected by a glycerol backbone (one single stereogenic center). Preliminary experiments performed by the scientific coordinator showed that a PLAN bearing an octyl chain has a strong tendency to form crystals with lattice-like phospholipid membranes, and no cellular toxicity. Such results encouraged the proposal of a research project based on two absolute novelties: the use of preferential enrichment as a major enantiomeric resolution of the crystals; the preparation of giant and large unilamellar vesicles (GUV and LUV) using enantiopure, racemic, and non-racemic PLAN. Such GUV and LUV will be further characterized by several techniques (fluorimetry, epifluorescence, confocal microscopy, TEM, etc.) and finally used to host sets of biologically relevant reactions (catalytic networks, genetic circuits, etc.) to understand whether the racemic composition of PLAN in the membrane plays a role in the reaction mechanism.



**Figure 1**. **A.** Left side: the general structure of **PLAN** and the structural analogies with archaea phospholipid; Right side: the working plan for the project **GiVe** and the specific tasks of each WP; **B.** Linear and convergent paths for the preparation of one of the possible long chain (±)-**PLAN**; chemical conditions envisaged for this project are in a first thought the following ones: *i*) p-nitrophenol, dry toluene, PhCH<sub>2</sub>NMe<sub>3</sub>Cl, reflux, o.n.; *ii*) Pd(OH)<sub>2</sub>/C/H<sub>2</sub>, MeOH, r.t., o.n.; *iii*) MeSCH<sub>2</sub>CH<sub>2</sub>COCl (MTPC), NaOH, CH<sub>2</sub>Cl<sub>2</sub>, r.t., o.n.; *iv*) R<sub>2</sub>SO<sub>3</sub>Me, acetone, 48h, reflux; R=Me, pMe-Ph, pCl-Ph); *v*) as for iii but with 3eq of MTPC; *vi*) as for *I*; **C.** Conditions *I* and *ii* have been used for the synthesis of **3a** and **4a** in 80% and quantitative conversion, respectively; **D.** Crystal structure of **3a** (orange) and **4a** (grey) as racemic mixtures, the compounds, together with **5a** showed no toxicity upon viability test on MC3T3 cells.<sup>9</sup>

## The preliminary results have been summarized in the following articles

## **Symmetry Breaking of Phospholipids**

M. Fiore,\* R. Buchet,

Symmetry **2020**, 12, 1488; doi:10.3390/sym12091488

Chemical Models for Understanding the Emergence of Homo-chirality of Phospholipids for Origin of Life Studies.

<u>Fryni Skorda, Carolina Chieffo</u>, **Michele Fiore\***, *Symmetry*, **2022**, 14, 2109 https://doi.org/10.3390/sym14102109

The Origin and Early Evolution of Life: Homochirality Emergence in Prebiotic Environments Carolina Chieffo, Anastasiia Shvetsova, Fryni Skorda, Augustin Lopez, and Michele Fiore\*

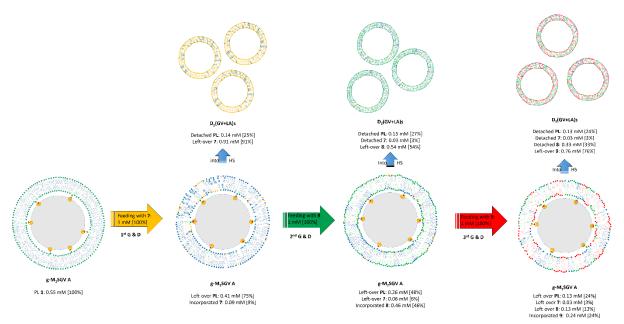
Astrobiology, 2023, 12, DOI: 10.1089/ast.2023.0007

Descrizione della attività scientifica - Summary of the research carried out in the last five years in Lyon

#### Research topic n° 1 Growth and division of lipid boundaries

The first list of articles concerns the following the **growth upon feeding and the eventual division of glass-supported giant vesicles**. The results obtained from 2017 to 2020 have been summarized into 2 scientific articles and 1 book chapter intended as a conference proceeding.

The concept: A cell lipid boundary's growth (followed by division) is a known phenomenon. In the origin of life, studies frame the study of this phenomenon as relevant for understanding how protocells have emerged and thus evolved from such inanimate mixtures called prebiotic. Growth and Division of lipid boundaries was with one exception,<sup>5</sup> carried out with non-prebiotic lipid boundaries often made of oleic acid fed with oleic acid or oleic acid sources see reference reported in ref <sup>1</sup>, however, no distinction from the original population of vesicles and the new generation of the vesicles. I decided to investigate in this direction by performing so-called "Growth and division" experiments on phospholipid boundaries using glass microsphere-supported phospholipid (DOPC) giant vesicles (GVs) fed with a fatty acid solution (oleic acid). The density difference between supported mother vesicles and newly formed daughter vesicles allowed their easy separation. Mass spectrometric analysis of the resulting mother and daughter GVs showed that the composition of both vesicle types was a mixture of originally supported phospholipids and added fatty acids reflecting the total composition of amphiphiles after the feeding process. I worked on this project in full autonomy selecting the phospholipid composition and the fatty acid based on previous literature and unpublished results of Monnard's (FLINT laboratory, ODENSE, Denmark). In the absence of any student in the lab, I have designed and carried out all the experiments, analysed each sample and collected images collected at the microscope. The main result is that under feeding conditions the membrane growth process (evagination, buds, filaments) was observed in detail by fluorescence microscopy on the surface of a tethered membrane that acted as "mother" vesicle thus, non-tethered ones. Thus, self-reproduction of phospholipid vesicles can take place under preservation of the lipid composition but with different aggregate sizes. This second published research took place from Fiore et al., Angew. Chem. Int. Ed. 2018 and represent the second stage of the ongoing research on the growth and division of tethered protocells. For the first time we have observed that the growth and the division of a protocell can be performed by sequential cycles (we have performed 3) favoring the exchange of material (i.e. genetic cross transfer/lipid content) between population of mothers and daughters vesicles. My main contribution has been to design all the experiments, perform the first microscopical analysis and train the students Fayolle, Lopez and Chieffo in this research activity of the group.



**Figure 1**. Graphical representation of the growth and division, thus recycling and growth and division of a second, thus a third generation of mother vesicles ( $M_{0^-3}SGVA$ ) and those that are considered daughter ones ( $D_{1-3}(GVs)$ ). Each color correspond to a different fatty acid: yellow, green and red (Myristic, oleic and myristoleic acids respectively). The n° of the objects that costitue the membrane correspond at the concentration found for each phospholipid/phospholipid mixtures (in blue) and each used fatty acid.<sup>6</sup>

In the third article, we have reported that the thethered membrane can be enriched with different and complex mixtures of phospholipids including egg yolk extracts and licitines from soya bean. The experiments carried out in ref <sup>1</sup> were successfully repeated and summarized in <sup>3</sup>.

This research activity is summarized in the following articles

## Glass Microsphere-Supported Giant Vesicles as Tools for Observation of Self-reproduction of Lipid Boundaries

M. Fiore\*, O. Maniti, A. Girard-Egrot, P-A Monnard and P. Strazewski *Angew. Chem. Int. Ed.*, **2018**, *57*, 282–286 (open access)

# Chemical Analysis of Lipid Boundaries after Consecutive Growth and Division of Supported Giant Vesicles. A. Lopez; D. Fayolle; M.Fiore\*; P. Strazewski - *iScience*, **2020** <a href="https://doi.org/10.1016/j.isci.2020.101677">https://doi.org/10.1016/j.isci.2020.101677</a> (open access)

## Following the Growth and Division of Lipid Boundaries by Using Glass Microsphere-Supported Protocells (2020)

A. Lopez, C. Chieffo, M. Fiore\*

In: Book Series: Lecture Notes in Bioengineering, S. Piotto, S. Concilio, L. Sessa, F. Rossi, Editors Publisher: Springer International PublishingPrint ISBN: 978-3-030-47704-2 (open acces)

## Research topic n 2: Prebiotic chemistry of amphiphiles in the frame of origin of life studies, vesicles formations and symmetry breaking

This research has been carried out from the beginning of my career in Lyon from 2014 to 2019. The general idea is that vesicles can be formed upon hydration when racemic phospholipids or naturally occurring analogs are formed under so-called prebiotic conditions (absence of enzymes, chiral

inducers...). Despite the lack of homo-chirality membrane formed yielding vesicles of various sizes that have been characterized by confocal microscopy and flow cytometry. These objects were able to host in the lumen, the void part of a vesicle, polar compounds including fluorescent polymers such as DNA and RNA. Furthermore and for the first time different giant vesicles produced from phospholipid mixtures as enantiopure, scalemic (non-racemic) or racemic ones were compared and tested for encapsulation studies suggesting that enantiopure mixtures are more performant. My main contribution is to conceptualize this research, inserted in a large research frame, on the investigation in prebiotic chemistry of phospholipids and phospholipids analogues. In addition, I have revised and upgraded two chemical pathways for the synthesis of racemic (but also enantiopure) phospholipid esters; Altamura et al;, article was prized in 2020 & 2021 as Editor's choice from Symmetry – MDPI, BASEL

### **Selected articles**

Crude phosphorylation mixtures containing racemic lipid amphiphiles self-assemble to give stable primitive compartments; D. Fayolle, E. Altamura, A. D'Onofrio, W. J. Madanamothoo, B. Fenet, F. Mavelli, R. Buchet, P. Stano\*, M. Fiore\* and P.Strazewski\* *Sci. Rep.*, **2017**, 7, 18106 (open access)

### Racemic phospholipids for origin of life studies

E. Altamura, A. Comte, A. D'Onofrio, C. Roussillon, D. Fayolle, R. Buchet, F. Mavelli, P. Stano, **M. Fiore,\*** P. Strazewski; *Symmetry* **2020**, *12*, 1108; doi:10.3390/sym12071108 (open access)

### Research topic n 3: Systems biology and ATP recognition

This research was carried out mainly by the former director od the MEM group – ICBMS –University of Lyon 1, Prof. René Buchet whit whom I have a good collaboration from the recruitment at the University of Lyon 1. My commitment in the early stage of this reserch was to analyse at the <sup>31</sup>P NMR the content of ATP, ADP, AMP and Pi that were digested by non-specific alkaline phosphatase (TNAP) enzyme and to produce calibration curves to quantify the content of the same molecules in murine aortic smooth muscle cell line (MOVAS cells) were transdifferentiated into chondrocyte-like cells in calcifying medium, containing ascorbic acid and  $\beta$ -glycerophosphate.

The main objective of this research study is the construction of energetically autonomous artificial protocells. The group of Prof. Mavelli, located at the University of Bari, Italy have embraced this research from several years. The obtained result is one of the most ambitious goals in bottom-up synthetic biology. In few words, we show an efficient manner to produce adenosine 5'-triphosphate (ATP) in hybrid multicompartment protocells. 11 The goal of synthetic biology is to simplify as much as possible some functions in a protocell starting from existing "tools" and recombining them in a phospholipid bilayer. In this research we have combined bacterial chromatophores from Rhodobacter sphaeroides to accomplish the photophosphorylation of adenosine 5'-diphosphate (ADP) to ATP, functioning as nanosized photosynthetic organelles when encapsulated inside artificial giant phospholipid vesicles. Thus, the ATP production and quantification was monitored by using a known but poor used fluorescent dye, based on modification at the C1 of the Rhodamine 6G. This probe result to be selective for ATP and not for ADP. My main contribution have been the design and the preparation (by using a novel synthetic pathway) of a synthetic probe based on the modification at C1 of Rhodamine 6G moiety. Altought the use of the probe was limited inside the research, it relevance, the novelty in the synthetic preparation, and the high specificity towards ATP recognition have been objects of further studies and became one of the subjects of the PhD program of Carolina Chieffo "Synthesis and use of clickable fluorophores for the analysis and study of biomolecular systems encapsulated into phospholipidic giant vesicles" of witch I am the PhD director (2019 - 2022). The efforts made during the PhD have been prized with the publication of a recent manuscript :

Figure 2. The structure of two ATP-sensors

Microwave-Assisted Syntheses of Rhodamine, Rhodol, and Fluorescein Derivatives
Carolina Chieffo, Emiliano Altamura, Guillaume Pilet, Saida Mebarek, Peter Strazewski, and Michele
Fiore\* ChemPlusChem, 2023, 88, e202300189

Hydrolysis of Extracellular ATP by Vascular Smooth Muscle Cells Transdifferentiated into Chondrocytes Generates Pi but Not PPi; Rene Buchet, Camille Tribes, Valentine Rouaix, Bastien Doumèche, **Michele Fiore**, Yuqing Wu, David Magne and Saida Mebarek; *Int. J. Mol. Sci.* **2021**, 22, 2948. <a href="https://doi.org/10.3390/ijms22062948">https://doi.org/10.3390/ijms22062948</a> (open access)

## Shedding light on the role of Na, K-ATPase as a phosphatase during matrix vesiclemediated mineralization

Heitor Gobbi Sebinelli, Luiz Henrique da Silva Andrilli, Bruno Zocaratto Favarin, Marcos Antonio Eufrasio Cruz, Maytê Bolean, **Michele Fiore**, <u>Carolina Chieffo</u>, David Magne, Andrea Magrini, Ana Paula Ramos, José Luis Millán, Saida Mebarek, Rene Buchet, Massimo Bottini and Pietro Ciancaglini – *Int. J. Mol. Sci.* **2022**, https://doi.org/10.3390/ijms232315072

Chromatophores Efficiently Promote Light-Driven ATP Synthesis and DNA 3 Transcription Inside Hybrid Multi-Compartment Artificial Cells

E. Altamura, P. Albanese, R. Marotta, F. Milano, **M. Fiore**, M. Trotta, P. Stano and F. Mavelli PNAS, 2021 Vol. 118 No. 7 e2012170118 (open access)

This research was carried out at the University of Bari, Italy. I was involved as main collaborator from 2016, and I was involved in the synthesis of a tailored fluorescent fluorophore specific for ATP recognition. In addition in 2022 this article was assigned the 1st Prize Cozzarelli Award

The aim if this research is to expand the library of available molecules for the chemical recognition and quantification of ATP during cellular chemical processes and cellular stress.

Research topic n 4. Cellular chartography by using rhodol-based molecular probes and confocal imaging: synthesis of lysoprobes

As part of Carolina Chieffo's thesis (defense on 12/12/2022, director: Michele Fiore) we extensively explored the state of the art on the research topic proposed here, and obtained two important results. First, the preparation of two specific fluorescent probes for targeting lysosomes. These probes were

tested in MC3T3-E1 (C57BL/6 mouse calvaria) osteoblast cells. Secondly, we determined that the best quantum yield among the different probes prepared is associated with a very little-known xanthene: Rhodol. Rhodol-lactam and its homolog (fluorescein-based) are the first examples of xanthenes, which gave a 100% preference for lysosomes and not for mitochondria. Their ability is based on a dynamic equilibrium between two different forms: a non-fluorescent spiro lactam and a fluorescent open ring conjugated form using EWG amines. Rhodols are now good candidates for obtaining lyso-trackers in terms of synthesis, purification, and quantum yields. The final goal of this project is therefore to extend the library of possible xanthene-lactam/xanthene amide (off/on) lyso-trackers using the rhodol molecular template. For this purpose, the synthesis of the starting rhodol methyl ester required an improvement compared to the synthetic routes presented in the literature: multi-step syntheses or syntheses under harsh conditions, both with the disadvantage of low yields. To carry out this first step it is necessary to retrace the synthesis of rhodol from a synthesis intermediate that is easy to prepare and possibly usable for the "tuning" of different LTs. We identified a good candidate in the rhodol methyl ester, which is prepared from phthalic anhydride and resorcinol. This intermediate, according to preliminary results obtained within the SysChem-CO2 team, showed that the synthesis of rhodol methyl ester is possible with better yields (>30-50%). The substitution of oxygen for the 3' carbon of rhodol and/or xhantenic oxygen can be used to extend the emission wavelength of rhodols.

This research topic has been prized with a fellowship for a PhD contract.

The results of this research topic are partially summarized in the following article

## A Comprehensive Characterization of "Off/On" Rhodol-based Lysosomal Tracker for Orthogonal Cellular Analysis by Confocal Imaging

<u>Carolina Chieffo, Emiliano Altamura</u>, Layth Ben Trad, Guillaume Pilet, Ofelia Maniti, Thierry Granjon, Saida Mabarek, Peter Strazewski, **Michele Fiore\*** - *ChemBioChem, e202200513*, https://doi.org/10.1002/cbic.202200513

### Research topic n 5. Vaccine carriers using synthetic outher membrane vesicles (S-OMV)

This article shows preliminary results obtained in the field of vaccine development 3.0. The main idea is to prepare outer membrane vesicles by combining in the same bilayer thioglycosides and non immunogenic naturally occurring phospholipids. Thio-glycosides have been mainly synthesized by TEC (thiol-ene) reaction and have been used, pure or in mixture with phospholipids to produce synthetic outer membrane vesicles. ELLA test showed a good binding capacity of the molecules. Two different lipid scaffolds have been used and prepared on purposes.

Figure 3. Lipid scaffolds used for the synthesis of Glycolipids in S-OMVs preparation

The results of this research topic are summarized in the following articles

## **Synthetic Outer Membrane Vesicles Bearing Tn Antigen**

<u>Carolina Chieffo</u>, Arnaud Comte, Peter Strazewski and **Michele Fiore\*** *Eur. J. Org. Chem.* **2023**, e202300820; doi.org/10.1002/ejoc.202300820

Towards the preparation of synthetic outer membrane vesicle models with micromolar affinity to wheat germ agglutinin using a dialkyl thioglycoside.

<u>D. Fayolle</u>, B. Doumèche, N. Berthet, O. Renaudet, P. Strazewski, **M. Fiore\*** *Beilstein J. Org. Chem.* **2019**, *15*, 937–946. doi:10.3762/bjoc.15.90

Those results allowed the LCO2 research group (<a href="https://www.icbms.fr/fr/equipe/20-lco2-html">https://www.icbms.fr/fr/equipe/20-lco2-html</a>), to participate to the consortium MSCA COFUND International Doctoral Programme - HORIZON-

ArchiFun: Architecture, function and dynamics in Life Sciences

Beneficiary: Université Claude Bernard Lyon 1

MSCA-2022-COFUND-01 no. 101126656