

## **Phylogenetic-guided bioprospection of the Italian flora: from the exploitation of bioactive phytochemicals to the study of chemo-evolutionary dynamics**

Stefano Negri<sup>1</sup>, Mauro Commisso<sup>1</sup>, Leonardo Bisson<sup>1</sup>, Carolina Ramos<sup>1</sup>, Gianluca Zorzi<sup>1</sup>, Fabio Pietrolucci<sup>1</sup>, Fabio Pinzauti<sup>1</sup>, Sebastiano Nigris<sup>2,3</sup>, Barbara Baldan<sup>2,3</sup>, Sebastiano Andreatta<sup>4</sup>, Daniele Zanini<sup>5</sup>, Roberto Fiorentin<sup>6</sup>, Maria Carmela Caria<sup>7</sup>, Alfredo Maccioni<sup>7</sup>, Emmanuele Farris<sup>7</sup>, Simonetta Bagella<sup>7</sup>, Federico Sgadari<sup>8</sup>, Rosario Schicchi<sup>8</sup>, Anna Geraci<sup>9</sup>, Alfredo Carratello<sup>10</sup>, Emanuela Martino<sup>11</sup>, Nicola Ardenghi<sup>12</sup>, Francesco Bracco<sup>11</sup>, Valeria Cavalloro<sup>11</sup>, Alice Fossati<sup>11</sup>, Linda Avesani<sup>1</sup> and Flavia Guzzo<sup>1\*</sup>

1 Department of Biotechnology, University of Verona, Strada Le Grazie 15, 37134 Verona, Italy

2 Department of Biology, University of Padova, Viale Colombo 3, 35131 Padova, Italy;

3 Centro di Ateneo Orto Botanico, Via Orto Botanico 15, 35123 Padova, Italy;

4 Museo Civico di Storia Naturale di Verona, Lungadige Porta Vittoria 9, 37129 Verona, Italy;

5 Orto Botanico del Monte Baldo, Strada Graziani 10, 37020 Ferrara di Monte Baldo (Verona), Italy;

6 Centro Biodiversità Vegetale e Fuori Foresta, Veneto Agricoltura, Via Bonin-Longare 4, 36030 Montebelluna Precalcino (Vicenza), Italy.

7 Department of Chemical, Physical, Mathematical and Natural Sciences, University of Sassari, Via Piandanna 4, 07100 Sassari, Italy;

8 Department of Agricultural, Food and Forest Sciences (SAAF), University of Palermo, Viale delle Scienze Ed. 4, 90123 Palermo Italy;

9 Department of Biological, Chemical and Pharmaceutical Sciences and Technologies (STEBICEF), University of Palermo, Viale delle Scienze Ed. 16, 90123 Palermo, Italy;

10 Centro Servizi Sistema Museale di Ateneo, University of Palermo, Via Lincoln 2, 90123 Palermo, Italy

11 Department of Earth and Environmental Sciences, University of Pavia, Via S. Epifanio 14, 27100 Pavia, Italy;

12 Orto Botanico Sistema Museale di Ateneo, Università degli Studi di Pavia, Via S. Epifanio 14, 27100, Pavia, Italy.

\*corresponding author: [flavia.guzzo@univr.it](mailto:flavia.guzzo@univr.it)

During their history, plants have evolved various physiological adaptations and a vast arsenal of biomolecules to thrive in diverse environments and coexist with other living organisms. The extensive diversity in terms of structures, functions, and bioactivities found within the specialized metabolism of plants represents a powerful asset for bioprospection-based drug discovery approaches. At the same time, it poses a significant challenge in understanding the chemo-evolutionary dynamics of plant biodiversity, intended as the intricate relationships between the distribution and synthesis of plant metabolites and the evolutive diversification of the various taxa of land plants.

In the frame of the National Biodiversity Future Center, dedicated to monitoring, conservation, restoration and valorization of biodiversity, we set up a wide bioprospection plan including about 700 plant species representing all the vascular and not vascular Italian flora. To cover the extensive phytochemical diversity expressed within it, species from all the Italian botanical families were selected on a phylogenetic basis, maintaining the original proportions among the various families (e.g., for the Angiosperms, in order: Asteraceae, Poaceae, Fabaceae, Rosaceae, etc.). Following their characterization through UPLC-HRMS, the species with the most interesting phytochemical profiles enter a downstream bioactivity screening program focused on non-communicable diseases and crop protection. This screening aims to identify specific phytochemicals or phytocomplexes that could be exploited to produce drugs, nutraceuticals, cosmetics and products for a more sustainable agriculture. Moreover, the comparison of all the plant species through untargeted metabolomics will be also performed to chart the specialized metabolisms through all the families of Italian flora in order to gain greater knowledge on the relationships of their occurrence and biosynthesis with the evolution of land plants.