

# Bioassay-guided identification of bioactive protein compounds from the Mediterranean demosponge *Tethya meloni*

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Further Information

## Publication History

Publication Date:

14 December 2016 (online)

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Marine natural products extracted from sponges represent a new source for drug discovery. Among marine organisms, the phylum Porifera is the most prolific for the production of pharmacologically active compounds, which are characterized by unique chemical structures [1]. Potential drug discovery targets include matrix metalloproteinases (MMPs), and in particular gelatinases A (MMP-2) and B (MMP-9), which are involved at different levels in the pathogenesis of several human diseases [2]. We used a simple method for preparing aqueous extracts from the Mediterranean demosponge *Tethya meloni* [3], which allowed the extraction of water-soluble compounds by homogenization of sponge tissue in phosphate buffered saline [4]. The analysis by SDS-PAGE showed a very rich protein pattern. Using a well-known in vitro model represented by lipopolysaccharides (LPS)-activated rat astrocytes, we demonstrated the capability of the sponge extract to inhibit the activity of MMP-2 and MMP-9 in a dose-dependent manner. In particular, astrocytes treated with the crude extract at the higher non-cytotoxic concentration of 60 µg/ml showed a 50% inhibition of MMP-2 and a 70% inhibition of MMP-9 in comparison with the positive control (LPS-activated astrocytes). To identify the bioactive compounds with anti-MMP activity, the crude extract was subjected to anion-exchange chromatography and the pools obtained by the different protein peaks were tested on LPS-activated astrocytes. We identified one fraction, which contains a major protein band of 30 kDa, which exhibited an 80% inhibition towards both MMP-2 and MMP-9, in comparison to positive control. In an effort aimed at the identification of the bioactive compounds with anti-MMP activity, this fraction was subjected to 2-D

electrophoresis. Results indicated the presence of about 10 spots at pI between 4.5 and 9.5; probably isoforms of the same protein. The identification of protein, which might be used for pharmaceutical applications, is now in course by MS-MS analysis.

Acknowledgements: Dr. Frine Cardone is acknowledged for sample collection, Dr. Marilena Larocca is acknowledged for technical support in the 2-DE analyses.

Keywords: Demosponge, aqueous extracts, bioactive compounds, matrix metalloproteinases.

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