Two PhD positions (36 months each) are available at the Department of Chemistry of the University of Milano in the frame of the Marie Skłodowska-Curie Innovative Training Network (ITN-ETN) “Peptide-Drug Conjugates for Targeted Delivery in Tumor Therapy” (MAGICBULLET) funded by the European Commission (Grant agreement no: 642004).

The two researchers, who will take part in the above project, will be enrolled by the University of Milano in the PhD Course of Chemistry, granting a PhD degree at the end of three years.

Goals of the network project
The ETN MAGICBULLET will 1) identify, modify, and validate tumor-selective peptides for known and new cell surface receptor targets (e.g. integrins, VEGFR, cadherins); 2) study different linker systems for release of the anticancer payloads at the appropriate site; 3) conjugate known and new anticancer agents or drugs to tumor-selective peptides; 4) investigate the biological activity in vitro and in vivo to demonstrate their efficacy. The combination of an array of tumor-selective peptides targeting different receptors and different uptake mechanisms with diverse antitumor drugs acting on different cellular targets is a powerful strategy to minimize potential risks and increase the efficacy. Because the number of receptors on tumor cells is limited, the combination of different target peptide – drug conjugates may enhance the bioactivity. The influence of the treatment schedule of such combination therapy on the antitumor activity will also be evaluated.

The common theme of the ETN will provide the young researchers with a unique portfolio of competences ranging from synthetic chemistry over medicinal chemistry to tumor biology. This warrants interdisciplinary training, supplemented by a well-balanced training in transferable skills. The close cooperation between 7 university groups, 2 public research institutes, and 5 industrial groups will enable young researchers to get insight into the research and development procedures and also to get into contact with potential future employers.

PhD student 1
PhD Project Title: Integrin ligands - anticancer drug conjugates.
PhD Project description: The PhD student will focus on the conjugation of integrin ligands (RGD peptidomimetics) to potent cytotoxic agents available within the consortium, via suitable “smart linkers”. Ideally, the conjugates will retain a strong affinity for their integrin receptor, which will allow for their selective delivery to tumor cells. Moreover, owing to the use of “smart linkers”, the conjugates will have a good plasma stability, which will dramatically reduce their systemic toxicity. The selective protease cleavage of the linkers within the tumor cell will allow the payload to display all of its potency against the target.
Planned secondments: Bayer Pharma AG, Wuppertal, 3 months, Linker strategies for the conjugation of RGD ligands to anticancer agents; Bielefeld University, 6 months, Conjugation of RGD ligands to highly cytotoxic agents.

PhD student 2
PhD Project Title: New tumor-selective peptidomimetic VEGFR and cadherin ligands.
PhD Project description: The PhD student will focus on (i) the design and synthesis of new peptidomimetics capable of targeting VEGFR, displaying anti-angiogenic and anti-lymphangiogenic activity and good plasma stability; (ii) the design and synthesis of new peptidomimetic cadherin ligands, able to inhibit homophilic cell-cell adhesion; (iii) the synthesis of dual-specific (hybrid) agents capable of simultaneously inhibiting both integrin αvβ3 and VEGFR or cadherin; (iv) the
conjugation of the most efficient tumor-selective compounds to potent cytotoxic agents available within the consortium.

**Planned secondments:** Heidelberg Pharma GmbH, 3 months, Linker strategies for the conjugation of VEGFR- and cadherin-ligands to anticancer agents; Bielefeld University, 6 months, Conjugation of Cadherin ligands to highly cytotoxic agents.

**Academic Supervisor**
Prof. Dr. Cesare Gennari, Università degli Studi di Milano, Dipartimento di Chimica
Website: [http://users.unimi.it/dpcorind/en/?page_id=9](http://users.unimi.it/dpcorind/en/?page_id=9)

**Eligibility and salary**
The positions are open to candidates of any nationality, as long as they fulfill the requirements set for the Early Stage Researchers (ESRs) funded by Marie Skłodowska-Curie actions:

1. Candidates who have already obtained a Ph.D. degree, or have more than 4 years of research activity (from the date when they have obtained a University diploma giving access to doctoral studies), are not eligible.
2. Researchers must not have resided or carried out their main activity (work, studies, etc.) in Italy for more than 12 months in the 3 years immediately prior to the date of appointment.


**Desired experience/Academic degree**
The ideal candidates must have a strong background in synthetic organic chemistry, with an interest in medicinal chemistry and an excellent knowledge of the English language. The applicants must have acquired a University diploma giving access to doctoral studies in Chemistry in the Country where the diploma was earned (typically a Master degree in Chemistry).

**Applications**
Those who wish to apply should submit their application via e-mail (e-mail address: [luca.pignataro@unimi.it](mailto:luca.pignataro@unimi.it)), along with (i) a one-page letter of motivation; (ii) a CV including relevant skills, experience and publication list; (iii) a copy of their University diploma. For EU Countries, the Diploma Supplement is recommended, see: [http://ec.europa.eu/education/tools/diploma-supplement_en.htm](http://ec.europa.eu/education/tools/diploma-supplement_en.htm)

Moreover, at least two recommendation letters are required. The applicant should ask her/his referees to send the letters separately and confidentially to the above e-mail address. The above e-mail address can also be used for informal enquiries regarding the project.

**Deadline:** the applications and the letters of recommendation sent by the referees must be **received by March 27, 2015**. Skype interviews will be organized for selected, short-listed applicants.

**Start date:** The expected start date of the fellowships is **June 1, 2015**.