

Samuele Cazzamalli, PhD

Active member of the Italian Chemical Society (26086, Med Chem Division)

H-Index: 18 (Google Scholar)

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WORK EXPERIENCE

July 2020 - Present	HEAD OF CHEMISTRY – Philochem, Zürich (Switzerland)
Jan 2018 – July 2020	RESEARCH SCIENTIST – Philochem, Zürich (Switzerland)

EDUCATION

Jan 2015 – Jan 2018	PH.D. – ETH Zürich, Institute of Pharmaceutical Sciences (Switzerland) Group of Prof. Dario Neri – Tumor targeting with Small Molecules and Antibodies
Sep 2009 – Sep 2014	MASTER OF SCIENCE – Medicinal Chemistry and Pharmaceutical Technologies, University of Milan (Italy) Group of Prof. Carlo De Micheli – Flow chemistry and biocatalysis

LANGUAGES

Italian	Native speaker
English	Fluent working proficiency
German	Limited working proficiency
Spanish	Fluent working proficiency

PUBLICATIONS

“Targeted interleukin-2 enhances the in vivo anti-cancer activity of Pluvicto™” Georgiev T., Principi L., Galbiati A., Gilardoni E., Neri D., Cazzamalli S. *Eur J Nucl Med Mol Imaging* **2024**; <https://doi.org/10.1007/s00259-024-06705-x>

“In vivo activation of FAP-cleavable small molecule-drug conjugates for the targeted delivery of camptothecins and tubulin poisons to the tumor microenvironment” Bocci M., Zana A., Principi L., Lucaroni L., Prati L., Gilardoni E., Neri D., Cazzamalli S., Galbiati A. *J Control Release* **2024**; 367:779.

“Ex vivo mass spectrometry-based biodistribution analysis of an antibody-Resiquimod conjugate bearing a protease-cleavable and acid-labile linker” Lopez Bisbal L., Ravazza D., Bocci M., Zana A., Principi L., Dakhel Plaza S., Galbiati A., Gilardoni E., Scheuermann J., Neri D., Pignataro L., Gennari C., Cazzamalli S., Dal Corso A. *Front Pharmacol* **2023**; <https://doi.org/10.3389/fphar.2023.1320524>

“Tumor-Targeted Interleukin 2 Boosts the Anticancer Activity of FAP-Directed Radioligand Therapeutics” Galbiati A., Dorten P., Gilardoni E., Gierse F., Bocci M., Zana A., Mock J., Cleasener M., Cufe J., Büther F., Schäfers K., Hermann S., Schäfers M., Neri D., Cazzamalli S., Backhaus P. *J Nucl Med* **2023**; 64:1934.

“Impact of library input on the hit discovery rate in DNA-encoded chemical library selections” Puglioli S., Oehler S., Prati L., Scheuermann J., Bassi G., Cazzamalli S., Neri D., Favalli N. *Chem Sci* **2023**; 14: 12026.

“A DNA-encoded chemical library based on chiral 4-amino-proline enables stereospecific isozyme-selective protein recognition” Oehler S., Lucaroni L., Migliorini F., Elsayed A., Prati L., Puglioli S., Matasci M., Schira K., Scheuermann J., Yudin D., Jia M., Ban N., Bushnell D., Kornberg R., Cazzamalli S., Neri D., Favalli N., Bassi G. *Nat Chem* **2023**; 15; 1431.

“A comparative analysis of Fibroblast Activation Protein-Targeted Small Molecule-Drug, Antibody-Drug, and Peptide-Drug Conjugates” Zana A., Puig-Moreno C., Bocci M., Gilardoni E., Di Nitto C., Principi L., Ravazza D., Rotta G., Prodi E., De Luca R., Neri D., Cazzamalli S. *Bioconj Chem* **2023**; <https://doi.org/10.1021/acs.bioconjchem.3c00244>.

“Deep Learning Approach for the Discovery of Tumor-Targeting Small Organic Ligands from DNA-Encoded Chemical Libraries” Torng W., Biancofiore I., Oehler S., Xu J., Xu J., Watson I., Masina B., Prati L., Favalli N., Bassi G., Neri D., Cazzamalli S., Feng JA. *ACS Omega* **2023**; <https://doi.org/10.1021/acsomega.3c01775>.

“Response to: GCP III is not the “off-target” for urea-based PSMA-ligands” Bassi G., Cazzamalli S., Oehler S., Lucaroni L., Georgiev T., Favalli N., Neri D., *Eur. J. Nucl. Med. Mol. Imaging* **2023**; <https://doi.org/10.1007/s00259-023-06302-4>.

“Cross-reactivity to glutamate carboxypeptidase III causes undesired salivary gland and kidney uptake of PSMA-targeted small-molecule radionuclide therapeutics” Lucaroni L., Georgiev T., Prodi E., Puglioli S., Pellegrino C., Favalli N., Prati L., Manz M., Cazzamalli S., Neri D., Oehler S., Bassi G. *Eur J Nucl Med Mol Im* **2023**; 50:957.

“Selective tumor targeting enabled by picomolar fibroblast activation protein inhibitors isolated from a DNA-encoded affinity maturation library” Puglioli S., Schmidt E., Pellegrino C., Prati L., Oehler S., De Luca R., Galbiati A., Comacchio C., Nadal L., Scheuermann J., Manz M., Neri D., Cazzamalli S., Bassi G., Favalli N. *Chem* **2022**; 2, 411-29.

“Fibroblast Activation Protein triggers release of drug payload from non-internalizing small molecule-drug conjugates in solid tumors” Zana A., Galbiati A., Gilardoni E., Bocci M., Millul J., Sturm T., Stucchi R., Elsayed A., Nadal L., Cirillo M., Roll W., Stegger L., Asmus I., Backhaus P., Schäfers M., Neri D., Cazzamalli S. *Clin Cancer Res* **2022**; doi: 10.1158/1078-0432.CCR-22-1788.

“Isolation of a Natural Killer Group 2D Small-Molecule Ligand from DNA-Encoded Chemical Libraries” Dakhel Plaza S., Galbiati A., Migliorini F., Comacchio C., Oehler S., Prati L., Scheuermann J., Cazzamalli S., Neri D., Bassi G., Favalli N. *ChemMedChem* **2022**; e202200350; doi: 10.1002/cmdc.202200350.

“Automated radiosynthesis, preliminary in vitro/in vivo characterization of OncoFAP-based radiopharmaceuticals for cancer imaging and therapy” Bartoli F., Elsinga P., Nazario Reali L., Zana A., Galbiati A., Millul J., Migliorini F., Cazzamalli S., Neri D., Slart Riemer H.J.A., Erba A.P. *Pharmaceuticals* **2022**; 15:958.

“Mass spectrometry-based method for the determination of the biodistribution of tumor-targeting small molecule-metal conjugates” Gilardoni E., Zana A., Galbiati A., Sturm T., Millul J., Cazzamalli S., Neri D., Stucchi R. *Anal Chem* **2022**; 94:10715.

“A novel dimeric FAP-targeting small molecule-radio conjugate with high and prolonged tumour uptake” Galbiati A., Zana A., Bocci M., Millul J., Elsayed A., Mock J., Neri D., Cazzamalli S. *J Nucl Med* **2022**; DOI: 10.2967/jnumed.122.264036

“Translational imaging of the fibroblast activation protein (FAP) using the new ligand [68Ga]Ga-OncoFAP-DOTAGA” Backhaus P., Gierse F., Burg M.C., Büther F., Asmus I.,

Dorten P., Cufe J., Roll W., Neri D., [Cazzamalli S.](#), Millul J., Mock J., Galbiati A., Zana A., Schäfers K.P., Hermann S., Weckesser M., Tio J., Wagner S., Breyholz H.-J., Schäfers M. *Eur J Nucl Med Mol Im* **2022**; 49:1822.

“Identification and Validation of New Interleukin-2 Ligands Using DNA-Encoded Libraries” Girona-Martinez A., Gorre E.M.D., Prati L., Gosalbes J.F., Dakhel S., [Cazzamalli S.](#), Samain F., Donckele E.J., Neri D. *J Med Chem* **2021**; DOI: 10.1021/acs.jmedchem.1c01693

“Specific Inhibitor of Placental Alkaline Phosphatase Isolated from a DNA-Encoded Chemical Library Targets Tumor of the Female Reproductive Tract” Bassi G., Favalli N., Pellegrino C., Onda Y., Scheuermann J., [Cazzamalli S.](#), Manz M.G., Neri D. *J Med Chem* **2021**; 64:15799.

“An ultra-high-affinity small organic ligand of fibroblast activation protein for tumor-targeting applications” Millul J., Bassi G., Mock J., Elsayed A., Pellegrino C., Zana A., Dakhel S., Nadal L., Gloger A., Schmid E., Biancofiore I., Donckele E.J., Samain F., Neri D., [Cazzamalli S.](#) *PNAS* **2021**; 118:16:e2101852118

“An attenuated targeted-TNF localizes to tumors in vivo and regains activity at the site of disease” Dakhel S., Lizak C., Matasci M., Mock J., Villa A., Neri D., [Cazzamalli S.](#) *Int J Mol Sci* **2021**; 22:10020

“Stereo- and regiodefined DNA-encoded chemical libraries enable efficient tumour-targeting applications” Favalli N., Bassi G., Pellegrino C., Millul J., De Luca R., [Cazzamalli S.](#), Yang S., Trenner A., Mozaffari N.L., Myburgh R., Moroglu M., Conway S.J., Sartori A.A., Manz M.G., Lerner R.A., Vogt P.K., Scheuermann J., Neri D. *Nat Chem* **2021**; 13:540.

“Antibody-based delivery of interleukin-9 to neovascular structures: therapeutic evaluation in cancer and arthritis” Gouyou B., Ongaro T., [Cazzamalli S.](#), De Luca R., Kerschenmeyer A., Valet P., Villa A., Neri D., Matasci M. *Exp Biol Med* **2021**; 246:940.

“Immunotherapy with immunocytokines and PD-1 blockade enhances the anticancer activity of small molecule-drug conjugates targeting carbonic anhydrase IX” Millul J., Krudewig C., Zana A., Plaza S.D., Puca E., Villa A., Neri D., [Cazzamalli S.](#) *Mol Cancer Ther* **2021**; 20:512.

“Sortase-mediated site-specific modification of interleukin-2 for the generation of a tumor-targeting acetazolamide–cytokine conjugate” Gouyou B., Millul J., Villa A., [Cazzamalli S.](#), Neri D., Matasci M. *ACS Omega* **2020**; 5:26077.

“A microdosing study with ^{99m}Tc-PHC-102 for the SPECT/CT imaging of primary and metastatic lesions in renal cell carcinoma patients” Kulterer O.C., Pfaff S., Wadsak W.,

Garstka N., Remzi M., Vranka C., Nics L., Bootz F., Cazzamalli S., Krall N., Neri D., Haug A.R. *J Nucl Med* **2020**; 62:360.

"Impact of ligand size and conjugation chemistry on the performance of universal chimeric antigen receptor T-cells for tumor killing" Pellegrino C., Nicholas Favalli, Sandholzer M., Volta L., Bassi G., Millul J., Cazzamalli S., Matasci M., Villa A., Myburgh R., Manz M.G., Neri D. *Bioconjug Chem* **2020**; 31:1775.

"Targeted enhancement of the therapeutic window of L19-TNF by transient and selective inhibition of RIPK1-signaling cascade" Dakhel S., Ongaro T., Gouyou B., Matasci M., Villa A., Neri D., Cazzamalli S. *Oncotarget* **2019**; 10:6678.

"The antibody-based delivery of interleukin-12 to solid tumors boosts NK and CD8 + T cell activity and synergizes with immune checkpoint inhibitors" Puca E., Probst P., Stringhini M., Murer P., Pellegrini G., Cazzamalli S., Huttmacher C., Gouyou B., Wulhfard S., Matasci M., Villa A., Neri D. *Int. J. Cancer* **2019**; 146:2518.

"A novel anti-cancer L19-interleukin-12 fusion protein with an optimized peptide linker efficiently localizes in vivo at the site of tumors" Ongaro T., Matasci M., Cazzamalli S., Gouyou B., De Luca R., Neri D., Villa A. *J. Biotechnol.* **2018**; 291:17.

"In vivo anti-tumor activity of a novel acetazolamide-cryptophycin conjugate for the treatment of renal cell carcinoma" Cazzamalli S., Figueras E., Pethő L., Borbély A., Steinkühler C., Neri D., Sewald N. *ACS Omega* **2018**; 3:14726.

"Chemically-defined antibody- and small molecule-drug conjugates for *in vivo* tumor targeting applications: a comparative analysis" Cazzamalli S., Dal Corso A., Widmayer F., Neri D. *J. Am. Chem. Soc.* **2018**; 140:1617.

"Versatile protein recognition by the encoded display of multiple chemical elements on a macrocyclic scaffold" Li Y., De Luca R., Cazzamalli S., Pretto F., Bajic D., Scheuermann J., Neri D. *Nat. Chem.* **2018**; 10:441.

"Enhanced therapeutic activity of non-internalizing small molecule-drug conjugates targeting carbonic anhydrase IX in combination with targeted interleukin-2" Cazzamalli S., Ziffels B., Widmayer F., Murer P., Pellegrini G., Pretto F., Wulhfard S., Neri D. *Clin. Cancer Res.* **2018**; 24:3656.

“Antibody-drug conjugates: targeting the tumor microenvironment” Dal Corso A., Cazzamalli S., Neri D. in *Innovations for Next-Generation ADCs*, Springer Nature **2018**; 299-319

“Targeted delivery of cytotoxic drugs: challenges, opportunities and new developments” Cazzamalli S., Dal Corso A., Neri D. *Chimia* **2017**; 71:712.

“Impact of a central scaffold on the binding affinity of fragment pairs isolated from DNA-encoded self-assembling chemical libraries” Bigatti M., Dal Corso A., Vanetti S., Cazzamalli S., Rieder U., Scheuermann J., Neri D., Sladojevich F. *Chem. Med. Chem.* **2017**; 12:1748.

“Protease-cleavable linkers modulate the anticancer activity of non-internalizing antibody-drug conjugates” Dal Corso A., Cazzamalli S., Gébleux R., Mattarella M., Neri D. *Bioconjug. Chem.* **2017**; 28:1826.

“Linker stability influences the anti-tumor activity of acetazolamide-drug conjugates for the therapy of renal cell carcinoma” Cazzamalli S., Dal Corso A., Neri D. *J Control Release.* **2017**; 246:39.

“Acetazolamide serves as selective delivery vehicle for dipeptide-linked drugs to renal cell carcinoma” Cazzamalli S., Dal Corso A., Neri D. *Mol Cancer Ther.* **2016**; 15:2926.

“An efficient continuous flow process for the synthesis of a non-conventional mixture of fructooligosaccharides” Zambelli P., Tamborini L., Cazzamalli S., Pinto A., Arioli S., Balzaretto S., Plou J. F., Fernandez-Arrojo L., Molinari F., Conti P., Romano D. *Food Chem.* **2016**; 190:607.

AWARDS

2019 **BEST PRE-CLINICAL PUBLICATION (RUN-UP)** – World ADC San Diego 2019

2018 **“YOUNG SCIENTIST” AWARD** – ETH Zürich

SELECTED PRESENTATIONS

(8 O F 2 2)

16th- 18th November 2023

“Small Molecule Therapeutics targeting Fibroblast Activation Protein in the tumor microenvironment” **EFMC International Symposium Chemical Biology, Basel (CH)** – Scheduled Talk

9 th - 11 th October 2023	“Small Molecule Therapeutics targeting Fibroblast Activation Protein in the tumor microenvironment” Festival of Biologics 2023, Basel (CH) – Talk
7 th - 8 th September 2023	“DNA-Encoded Chemical Libraries for the discovery of highly potent tumor-targeting ligands and for the development of anti-cancer Small Molecule Therapeutics” 11th International DNA-Encoded Chemical Library Symposium, Zurich (CH) – Talk
21 st - 24 th May 2023	“Drug Discovery with DNA-encoded Libraries (DEL)” European Workshop in Drug Synthesis, Siena (ITA) – Talk
25 th - 26 th August 2022	“Small Molecule Therapeutics as an alternative to Peptide Therapeutics: a clean strategy to delivery bioactive payloads to tumors” Peptide Therapeutic Forum, Basel (CH) – Talk
2 nd - 5 th March 2020	“Small Molecule-Drug Conjugates: Getting Small to Enhance Targeting” 10th World ADC, London (UK) – Talk
12 th - 15 th November 2018	“Small ligands for the imaging and the treatment of solid tumors in combination with targeted cytokines” 8th World ADC, San Diego (California) – Talk
26 th - 28 th March 2018	“Getting small to enhance targeting: non-internalizing small molecule-drug conjugates for the treatment of solid tumors” 8th World ADC, Berlin (Germany) – Talk