CURRICULUM VITAE

FORMATO EUROPEO/EUROPEAN FORMAT

PERSONAL INFORMATION

Name, Surname	Sonia Covaceuszach
Address	
House number, street name, postcode, city, country	Via Pasiano 17 33037 Passons – Pasian di Prato -Udine- (Italy)
Telephone	+39-3381144295
E-mail	sonia.covaceuszach@ic.cnr.it
Nationality	Italian
Place and Date of birth	Udine, 18/02/1972

WORK EXPERIENCE

Se dipendente CNR indicare:

N. MATRICOLA 14599
QUALIFICA RICERCATORE
LIVELLO 03

Dates (from – to)	**From 2012 to the present date**
Name and address of employer	C.N.R. - Istituto di Cristallografia - Unità Organizzativa di Supporto Trieste, Area Science Park, Basovizza, Strada Statale14, km 163.5, 34149 Trieste
Type of business or sector	Government institution
Occupation or position held	Researcher – permanent position
Main activities and responsibilities	Research activity on bacterial pathogens () to develop effective anti-microbial drugs. Research activity on transcriptional factors to develop effective anti-tumoral strategies. Research activities in the field of neurotrophins. Expression, refolding and purification; bioinformatic analysis and molecular dynamics; structural and functional studies of neurotrophins, proneurotrofins and their receptors and natural ligands. Structural and functional studies of mutant pailess NGF and TrkA. Structural and functional studies on matrix proteins (i.e. dystroglycan and agrin) and their pathological mutants associated to genetic diseases. Expression, purification and biophysical, functional and structural characterization.
Dates (from – to)	**From 2008 to 2012**
Name and address of employer	Rottapharm Biotech, Area Science Park, Basovizza, Strada Statale14, km 163.5, 34149 Trieste,
Type of business or sector	Company in the field of biotechnology
Occupation or position held	Senior Scientist, Head of the Protein Science Sector – permanent position
Main activities and responsibilities	Research activities in the field of design, selection and development of therapeutic antibodies against osteoarthritis and pain. Structural analysis of the targets, expression, refolding and purification of the antibodies selected by IACT (Intracellular Antibody Capture Technology) in scFv and Fabs formats, in vitro biophysical characterization and validation. Modeling of the most promising candidates and design humanized version by CDR grafting.
Dates (from – to)	**From 2006 to 2008**
Name and address of employer	Lay Line Genomics, Area Science Park, Basovizza, Strada Statale14, km 163.5, 34149 Trieste
Occupation or position held Type of business or sector	Company in the field of biotechnology Senior Scientist – permanent position
Main activities and responsibilities	Research activities in the NGF unit as a senior scientist. Structural and functional studies on a therapeutic variant hNGF and on pailess NGF mutants (in vitro binding assays and functional assays on cell cultures). Research activities in the Antibody Unit. Modeling studies of an anti-CD40 antibody and design a humanized version by CDR-grafting. Structural analysis of potential targets of therapeutic interest in the field of pain. Identification of key regions in order to design a chimeric protein based on a scaffold protein in order to select the function blocking antibodies. Expression, refolding and purification of the antibodies in scFv format and in vitro functional characterization. Expression, purification and biophysical characterization of the native and chimeric scaffold protein.

Dates (from – to)	**From 2002 to 2005**
Name and address of employer	*Lay Line Genomics, Area Science Park, Basovizza, Strada Statale14, km 163.5, 34149 Trieste*
Type of business or sector	Company in the field of biotechnology
Occupation or position held	Collaborator
Main activities and responsibilities	Research activities in the neuroantibody unit as a junior scientist. Development of a new methodology of antibody humanization based on experimental structural information and its experimental validation on two antibodies neutralizing the interaction between NGF and TrkA, by in vitro binding assays and by functional assays on cell cultures. Both humanized versions have been licensed, respectively the anti-TrkA to Bioxell (and subsequently to GenMark) and the anti-NGF to PanGenetics (and then to Abbot). SAXS studies (Small Angle X-ray Scattering) on hNGF and its complex with the neutralizing antibody in Fab format in collaboration with the group of Dr. D. Svergun SAXS line at the EMBL synchrotron DESY, Hamburg, Germany.

EDUCATION AND TRAINING

Dates (from – to)	**From 1997 to 2002**
Name and type of organization providing education and training	*ISAS (Superior School of Advanced studies), Trieste (Italy)*
Principal subjects occupational skills covered	*Project in the field of neurotrophins, aimed to the characterization at the molecular level of the interaction between NGF and its receptor TrkA through structural studies of two neutralizing antibodies, which specifically block this interaction. Thesis entitled: "Insights into NGF-TrkA interaction: crystal structures of two blocking antibodies " under the supervision of Prof A. Cattaneo and Dr D. Lamba.* Main techniques in the field of Molecular Biology, Expression, purification and biophysical characterization of Recombinant Proteins, Protein Crystallization and-X ray Crystallography.
Title of qualification awarded	*Doctor Phylosophiae in Biophysics*
Level in National classification	*cum laude.*
Dates (from – to)	**From 1991 to 1997**
Name and type of organisation providing education and training	*University of Trieste, (Italy)*
Principal subjects occupational skills covered	*Thesis in Molecular and Cellular Biology, entitled: "Study on a possible role of factor HMGI-C in transcriptional regulation" under the supervision of Prof. G. Manfioletti and Dr. F. Mantovani.* Main techniques in the fields of Molecular and Cellular Biology
Title of qualification awarded	*Degree (MS.) in Biological Sciences*
Level in National classification	*110/110 cum laude*
Dates (from – to)	**From 1986 to 1991**
Name and type of organisation providing education and training	Liceo Scientifico "N. Copernico", Udine, (Italy)
Title of qualification awarded	High School Diploma
Level in National classification	58/60

RESEARCH ACTIVITIES

Research sectors	Protein Science. Structural Biology. Bioinformatics.

Recent Scientific Activities.

Research activity on relevant targets of bacterial pathogens to develop effective anti-microbials.
Research activity on human transcription factors to develop anti-tumoral drugs.
Structural and functional studies of proneurotrophins, neurotrophins and ligands.
Structural and functional studies on extracellular matrix protein associated to genetic diseases.

Teaching

Contract Professor: "*Tecniche di indagine biostrutturale con luce di sincrotrone*"
A.A. 2019-2022 (I Semestre, 24 hours)
Laurea Magistrale –Biotecnologie Mediche
Università degli Studi di Trieste
"BIOSAXS"
February 2018
"Advanced methods for the integration of diverse structural data (3rd edition)"
"INSTRUCT practical course", Firenze
"Heterologous protein expression: an overview"
November 2002.
PhD in Structural and functional Genomics,
SISSA/ISAS, Trieste
"Baculovirus expression system"
April 1998.
(course: Biologia Cellulare), Facoltà di Scienze Biologiche,
Università degli Studi di Trieste

Recent Seminars

"Insights on the structural determinants of proBDNF V66M variant, a modifier in neuropsychiatric disorders severity." September 2022, 4 Joint AIC-SILS Conference, Trieste
""Unravelling the Primary Structural Determinants Essential for Proneurotrophins Biological Functions by a Combined Evolutionary and Structural Approach", May 2022, II Joined Workshop between the Institute of Crystallography (CNR) and the Department of Pharmacy – Pharmaceutical Sciences (UNIBA)
"Disclosing the Major Structural Determinants Essential for Proneurotrophins Biological Functions", October 2021. I° Conference on Crystallography, Structural Chemistry and Biosystems, Catania
"*A combined evolutionary and structural approach to disclose the primary structural determinants essential for proneurotrophins biological functions." June 2021,* 2nd AIC-BMM.

Books and Articles

1. Covaceuszach S, Peche LY, Konarev PV, Grdadolnik J, Cattaneo A, Lamba D. (2022). Untangling the Conformational Plasticity of V66M Human proBDNF Polymorphism as a Modifier of Psychiatric Disorder Susceptibility. Int J Mol Sci.;23(12):6596.
2. **Covaceuszach S**, Peche LY, Konarev PV, Lamba D. A combined evolutionary and structural approach to disclose the primary structural determinants essential for proneurotrophins biological functions. Comput Struct Biotechnol J. (2021) *May 7*;19:2891-2904.
3. Paoletti F, Merzel F, Cassetta A, Ogris I, **Covaceuszach S**, Grdadolnik J, Lamba D, Golič Grdadolnik S. Endogenous modulators of neurotrophin signaling: Landscape of the transient ATP-NGF interactions. Comput Struct Biotechnol J. (2021) May 7;19:2938-2949
4. Bez C., **Covaceuzach S.**, Bertani I., Choudhary K.S., Venturi V. LuxR solos from environmental fluorescent pseudomonads. mSphere (2021) Mar 31;6(2):e01322-20.
5. Maso L., Trande M., Liberi S., Moro G., Daems E., Linciano S., Sobott F., **Covaceuszach S.**, Cassetta A., Fasolato S., Moretto L.M., De Wael K., Cendron L., Angelini A. Unveiling the binding mode of perfluorooctanoic acid to human serum albumin. Protein Science (2021) Apr;30(4):830-841.
6. Mosquito S., Meng X., Devescovi G., Bertani I., Geller A.M., Levy A., Myers M.P., Bez C., **Covaceuszach S.**, Venturi V. LuxR Solos in the Plant Endophyte *Kosakonia* sp. Strain KO348. Appl Environ Microbiol. 2020 Jun 17;86(13):e00622-20.
7. Moro G., Bottari F., Liberi S., **Covaceuszach S.**, Cassetta A., Angelini A., De Wael K., Moretto L.M. Covalent immobilization of delipidated human serum albumin on poly(pyrrole-2-carboxylic) acid film for the impedimetric detection of perfluorooctanoic acid. Bioelectrochemistry. (2020) Aug;134:107540.
8. Signorino G., **Covaceuszach** S., Bozzi M., Hübner W., Mönkemöller V., Konarev P.V., Cassetta A., Brancaccio A., Sciandra F. A dystroglycan mutation

(p.Cys667Phe) associated to muscle-eye-brain disease with multicystic leucodystrophy results in ER-retention of the mutant protein. Hum Mutat. (2018) Feb;39(2):266-280.
9. **Covaceuszach** S., Bozzi M., Bigotti M.G., Sciandra F., Konarev P.V., Brancaccio A., Cassetta A. "The effect of the pathological V72I, D109N and T190M missense mutations on the molecular structure of α-dystroglycan." PLoS One. (2017) Oct 16;12(10):e0186110. doi: 10.1371/journal.pone.0186110. eCollection 2017.
10. **Covaceuszach S**., Bozzi M., Bigotti M.G. , Sciandra F., Konarev P., Brancaccio A**.,** Cassetta A**.** Structural flexibility of human alpha-Dystroglycan. FEBS Open bio 7:1064 (2017), DOI: 10.1002/2211-5463.12259.
11. Devescovi G., Kojic M., **Covaceuszach** S., Cámara M., Williams P., Bertani I., Subramoni S., Venturi V. Negative Regulation of Violacein Biosynthesis in *Chromobacterium violaceum*. Front Microbiol. (2017) 8:349.
12. Paoletti F., de Chiara C., Kelly G., **Covaceuszach** S., Malerba F., Yan R., Lamba D., Cattaneo A., Pastore A. Conformational Rigidity within Plasticity Promotes Differential Target Recognition of Nerve Growth Factor. Front Mol Biosci. (2016) 3:83
13. Passos da Silva D., Kumar Patel H.,González J.F., Devescovi G., Meng X., **Covaceuszach S**., Lamba D., Subramoni S., Venturi V. *Studies on synthetic LuxR solo hybrids.* Front. Cell. Infect. Microbiol. (2015) 18;5:52
14. Bozzi M., Cassetta A**.,** **Covaceuszach S**., Bigotti M.G. , Bannister S., Hübner W., Sciandra F.,Lamba D., Brancaccio A. "The Structure of the T190M Mutant of Murine alpha-Dystroglycan at High Resolution: Insight into the Molecular Basis of a Primary Dystroglycanopathy." PLoS One (2015) 10(5):e0124277
15. **Covaceuszach S**., Konarev P. V., Paoletti F., Krastanova I., Svergun D.I., Lamba D., Cattaneo A. "The conundrum of the high-affinity NGF binding site formation unveiled?". Biophysical J. (2015) 108(3):687
16. Kumar Patel H., Ferrante P., **Covaceuszach S.**, Lamba D., Scortichini M., Venturi V. The kiwifruit emerging pathogen *Pseudomonas syringae* pv. *actinidiae* does not produce AHLs but possesses three LuxR solos. PLoS One (2014) 9(1):e87862
17. **Covaceuszach S.**, Degrassi G., Venturi V., Lamba D. "Structural insights on a novel interkingdom signaling circuit by cartography of the ligand-binding sites of the homologous LuxR-family." International Journal of Molecular Science (2013) 14(10):20578
18. Corbalan N., Runti G., Adler C., **Covaceuszach S.**, Ford R., Lamba D., Beis K., Scocchi M., Vincent P.A. "Functional and structural study of the dimeric inner membrane protein SbmA." J. Bacteriol. (2013) 195(23):5352
19. Chiusaroli R., Visentini M., Galimberti C., Casseler C., Mennuni L., **Covaceuszach S.**, Lanza M., Ugolini G., Caselli G., Rovati L.C., Visintin M. "Targeting of ADAMTS-5's ancillary domain with the recombinant mAb CRB0017 ameliorates disease progression in a spontaneous murine model of osteoarthritis." Osteoarthritis and Cartilage (2013), Aug 15. doi:pii: S1063-4584(13)00919-9. 10.1016/j.joca.2013.08.015.
20. **Covaceuszach S**., Marinelli S., Krastanova I., Ugolini G., Pavone F., Lamba D., Cattaneo A. "Single cycle structure-based humanization of an anti-nerve growth factor therapeutic antibody." PLoS One (2012) 7(3):e32212
21. Capsoni S., **Covaceuszach S.**, Marinelli S., Ceci M., Bernardo A., Minghetti L., Ugolini G., Pavone F., Cattaneo A. Taking pain out of NGF: a "painless" NGF mutant, linked to hereditary sensory autonomic neuropathy type V, with full neurotrophic activity. PLoS One 28;6(2):e17321 (2011).
22. **Covaceuszach S**., Capsoni S., Marinelli S., Pavone F., Ceci M., Ugolini G., Vignone D., Amato G., Paoletti F**.,** Lamba D., Cattaneo, A. "In vitro receptor binding properties of a "painless" NGF mutein, linked to Hereditary Sensory Autonomic Neuropathy type V". Biochemical Biophysical Research Communications 391, 824-829 (2010).
23. **Covaceuszach S**., Capsoni S., Ugolini G., Spirito F., Vignone D., Cattaneo A. Development of a non invasive NGF-based therapy for Alzheimer's disease. *Curr Alzheimer Res*. 6(2), 158-70 (2009).
24. Capsoni S., **Covaceuszach S**., Ugolini G., Spirito F., Vignone D., Stefanini B., Amato G., Cattaneo A. Delivery of NGF to the Brain: Intranasal versus Ocular Administration in Anti-NGF Transgenic Mice. *J Alzheimers Dis.* 16(2), 371-388 (2009).
25. Paoletti F., **Covaceuszach S**., Konarev P.V., Gonfloni S., Malerba F., Schwarz E., Svergun D.I., Cattaneo A., Lamba D. Intrinsic structural disorder of mouse proNGF. *Proteins.* 75(4), 990-1009 (2009).
26. **Covaceuszach S**., Cassetta A., Konarev P.V., Gonfloni. S., Rudolph R., Svergun D.I., Lamba D., Cattaneo A. Dissecting NGF interactions with TrkA and p75 receptors by structural and functional studies of an anti-NGF neutralizing antibody. *J Mol Biol.* 381(4), 881-9 (2008).

27. Ugolini G., Marinelli S., **Covaceuszach S**., Cattaneo A., Pavone F. The function neutralizing anti-TrkA antibody MNAC13 reduces inflammatory and neuropathic pain. *Proc Natl Acad Sci U S A*. Feb 20;104(8):2985-90 (2007).
28. Paoletti F., Konarev P. V., **Covaceuszach S**, Schwarz E., Cattaneo A., Lamba D., Svergun D. I. Structural and functional properties of mouse proNGF. *Biochem Soc Trans.* 34(4), 605-6 (2006).
29. Ugolini G., **Covaceuszach S.**, Paoletti F., Visintin M., Lamba D., Cattaneo A. "Novel recombinant antibodies against AD biomarkers linked to neurotrophin signalling as potential diagnostic tools" Alzheimer & Dementia 2, S357 (2006).
30. **Covaceuszach S.**, Cattaneo A., Lamba D. Neutralization of NGF-TrkA receptor interaction by the novel antagonistic anti-TrkA monoclonal antibody MNAC13: A structural insight. *Proteins* 58(3), 717-727 (2005).
31. Brancucci A., Kuczewski N., **Covaceuszach S**., Cattaneo A., Domenici L. Nerve growth factor favours long-term depression over long-term potentiation in layer II-III neurones of rat visual cortex. *J Physiol.* 559, 497-506 (2004).
32. **Covaceuszach S**., Cassetta A., Cattaneo A., Lamba D. Purification, crystallization and X-ray diffraction analysis and phasing of a Fab fragment of monoclonal neuroantibody alphaD11 against nerve growth factor. *Acta Crystallogr D Biol Crystallogr* 60, 1323-1327 (2004).
33. Garaci E, Aquaro S, Lapenta C, Amendola A, Spada M, **Covaceuszach S**, Perno CF, Belardelli F. Anti-nerve growth factor Ab abrogates macrophage-mediated HIV-1 infection and depletion of CD4+ T lymphocytes in hu-SCID mice. *PNAS* 100, 8927-8932 (2003).
34. Tropea D., Capsoni S., **Covaceuszach S**., Domenici L., Cattaneo A. Rat visual cortical neurones express TrkA NGF receptor. *Neuroreport* 13, 1369-1373 (2002).
35. Margotti E., Covaceuszach S., Tongiorgi E., Cattaneo A., Domenici L. TRKB signalling controls the expression of N-methyl-d-aspartate receptors in the visual cortex. *Eur J Neurosci* 16, 1067-1074 (2002).
36. **Covaceuszach S**., Cattaneo A., Lamba D. Purification, crystallization and preliminary X-ray analysis of the Fab fragment from MNAC13, a novel antagonistic anti-tyrosine kinase A receptor monoclonal antibody. *Acta Crystallogr D Biol Crystallogr* 57, 1307-1309 (2001).
Mantovani F., **Covaceuszach S**., Rustighi A., Sgarra R., Heath C., Goodwin G.H. and Manfioletti G. Nf-kappaB mediated transcriptional activation is enhanced by the architectural factor HMGI-C. *Nucleic Acid Research* 26, 1433-1439 (1998).

ADDITIONAL INFORMATION:

PATENTS

Pub. No.: WO/2005/061540 International Application No.: PCT/IT2004/000722
Publication Date: 07.07.2005 International Filing Date: 23.12.2004
Applicants: LAY LINE GENOMICS S.P.A. [IT/IT];. SCUOLA INTERNAZIONALE SUPERIORE DI STUDI AVANZATI-SISSA [IT/IT].
Inventors: CATTANEO, Antonino; (IT). COVACEUSZACH, Sonia; (IT). LAMBA, Doriano; (IT).
Title: METHOD FOR THE HUMANIZATION OF ANTIBODIES AND HUMANIZED ANTIBODIES THEREBY OBTAINED
Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW. African Regional Intellectual Property Org. (ARIPO) (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW). Eurasian Patent Organization (EAPO) (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM). European Patent Office (EPO) (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR). African Intellectual Property Organization (OAPI) (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

RECENT POSTERS

1. Tosto R, Di Natale G, Sabatino G, Giuffrida ML, Zimbone S, **Covaceuszach S**, Pappalardo G. "Porphyrin-KLVFF: synthesis and neuroprotection action in Alzheimer's disease". International Symposium on Pathomechanisms of Amyloid Diseases, 2022
2. Paoletti F, Merzel F., Cassetta A., Ogris I., **Covaceuszach S**, Grdadolnik J, Lamba D, Golič Grdadolnik S. "Weak binding of ATP to the Nerve Growth Factor: a new modulation of neurotrophin signaling?" XIIth International conference "NMR: a tool for biology" Institut Pasteur, 2022
3. **Covaceuszach S**, Peche LY, Arduin S, Myers MP, Venturi V, Cassetta A. "Structural determinants of quorum sensing specificity vs promiscuity" I° Conference on Crystallography, Structural Chemistry and Biosystems, Catania*, 2021.*
4. Paoletti F., Merzel F., Cassetta A., Ogris I**, Covaceuszach S.,** Grdadolnik J**.,** Lamba D., Golič Grdadolnik S. *"Landscape of the transient binding interactions of Nerve Growth Factor with ATP as endogenous modulator of neurotrophin signaling",* CCPN 2021 Conference*,* Ambleside (UK), August 2021
5. **Covaceuszach S.,** Peche L.Y., Arduin S., Myers M.P., Venturi V., Cassetta A. "Quorum sensing LuxR promiscuity vs specificity: a structural perspective ", S4SAS Conference, Diamond (UK) 2020.
6. Sciandra F., Bozzi M., Bigotti M.G., Cassetta A., **Covaceuszach S.**, Hübner W., , Huser T., Eberle C.A., Niemir N., Blaess S., Brancaccio A. "A primary dystroglycanopathy causing muscle-eye-brain disease with multicystic leukodystrophy: from cellular and biochemical analysis to a mouse model", *MYOLOGY 2019,* Bordeaux, 2019.
7. Paoletti F, Ogris I,**Covaceuszach S**, Cassetta A., Lamba D, Grdadolnik J, Golič Grdadolnik S. ATP binding to the Nerve Growth Factor: a molecular switch for neurotrophins signaling? EFMC-ISMC 2019 - XXVI EFMC International Symposium on Medicinal Chemistry Dobrna (Poland), 2019.
8. Cassetta A., **Covaceuszach S.**, Sciandra F., Bozzi M., Bigotti M.G., Hübner W., Brancaccio A. Molecular and structural basis of dystroglycanopathies. Conferenza di Dipartimento di Scienze Chimiche e Tecnologie dei Materiali Bressanone, Italy, 2019.
9. Paoletti F, Ogris I,**Covaceuszach S**, Lamba D, Golič Grdadolnik S. *Insights into the Nerve Growth Factor / endogenous ligands binding mechanism.* EFMC-ISMC 2018 - XXV EFMC International Symposium on Medicinal Chemistry Ljubljana (Slovenia), 2018.
10. Paoletti F, Ogris I, **Covaceuszach S**, Lamba D, Golič Grdadolnik S *The binding of ATP to the Nerve Growth Factor: a new mechanism for neurotrophins signaling.* 7th Murnau Conference "New Frontiers in Structural Biology". Murnau, Germany, 2018.
11. **Covaceuszach S**., Bozzi M., Konarev P.V., Bigotti M.G., Sciandra F, Brancaccio A. Cassetta A., The molecular basis of α-dystroglycan hypoglycosylation: a crystallographic and SAXS study. 15th Naples Workshop on bioactive peptides, Napoli, Italy, 2016.
12. Bozzi M., Sciandra F, Bigotti M.G., Cassetta A., **Covaceuszach S.**, Konarev P.V., Brancaccio A. Insights into the structure of the N-terminal region of α-dystroglycan: a concerted crystallographic and SAXS study. *Matrix Biology* Europe Conference. *Athens,* Greece, 2016.