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Centro Singular de Investigación en Química Biolóxica e Materiais Moleculares

Conferencia: *Retro-translocation of proteins from the ER to the cytosol*

Oscar R. Burrone

ICGEB – Trieste - Italy

26/04/13

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Aula de Seminarios do CIQUS

12:15 h

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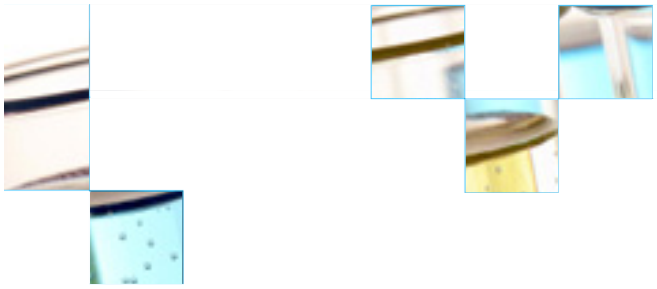

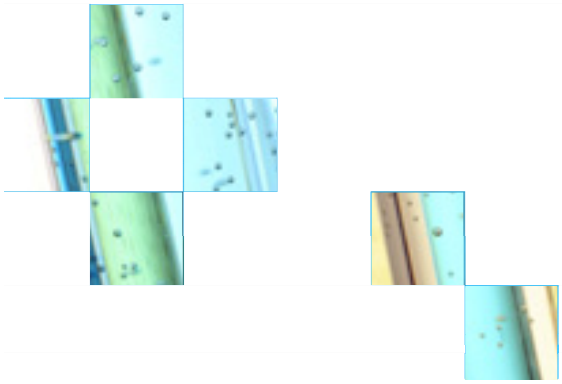

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CURRICULUM VITAE

Personal data:

Name: Oscar R. BURRONE

Born: August 11th, 1948, Argentina.

Work Address: International Centre for Genetic Engineering and Biotechnolgy (ICGEB), Padriciano 99, 34012 Trieste, Italy.

Education

1975: Bachellor in Chemical Sciences, Faculty of Sciences, University of Buenos Aires, Argentina
1979: Ph.D. in Biological Chemistry, Faculty of Sciences, University of Buenos Aires, Argentina

Position:

Senior Scientist and Group Leader of the Molecular Immunology Group of the International Centre for Genetic Engineering and Biotechnology,Trieste, Italy (ICGEB-Trieste).

Career History

Present

Since 1990 Senior Scientist and Group Leader, Molecular Immunology Group, ICGEB-Trieste
Since 1997 Co-ordinator of the PhD Course in Molecular Genetics and Biotechnology of the ICGEB-Trieste
Since 1999 Professor of Molecular Immunology, School of Medicine, Università di Trieste, Italy.

Past

1999-2010 Professor of Molecular Immunology, Scuola Normale Superiore di Pisa, Italy.

1998-2006 Lecturer of Biological Sciences, Master on Science Communication, International School for Advanced Studies, Trieste, Italy.
1986: Visiting Research Scientist, Department of Medical Virology, Biomedicum Center, University of Uppsala, Uppsala, Sweden.
1985-1989: Member of the Executive Committee of the National Program of Biotechnology, Ministry of Science and Technology, Buenos Aires, Argentina.
1985-1993: Assistant Professor, Instituto de Investigaciones Bioquímicas, Faculty of Sciences, University of Buenos Aires, Argentina.
1983-1990: Head of the Molecular Immunology and Virology Group, “Instituto Luis F. Leloir de Investigaciones Bioquimicas”, "Fundación Campomar", Buenos Aires, Argentina.
1983-1992: Scientific Career Member of the National Research Council (CONICET), Argentina.
1982: Visiting Scientist, EMBO Laboratory, Heidelberg, Germany.
1981-1983: Staff Research Scientist, MRC Laboratory of Molecular Biology, Division of Protein and Nucleic Acid Chemistry, Cambridge, England.
1979-1981: Post-doctoral research fellow, MRC Laboratory of Molecular Biology, Division of Protein and Nucleic Acid Chemistry, Cambridge, England.
1974-1979: Pre-doctoral research fellow, Instituto de Investigaciones Bioquimicas, "Fundación Campomar", and Faculty of Sciences, University of Buenos Aires, Buenos Aires, Argentina.

Scientific interests

Research interests focus in two major areas: immunology and virology.
-Protein engineering of antibody molecules
-DNA based vaccines
-Mechanism of ER to cytosol retro-translcoation
-Cross-presentation receptors of dendritic cells.
-Molecular Biology of rotavirus replication

Fellows Supervisions

PhD thesis, 28 students
Graduate thesis, 15 students

List of Publications (last 10 years)

Anti-idiotypic antibodies induced by genetic immunization are directed exclusively against combined V_L/V_H determinants.
Federica Benvenuti and Oscar R. Burrone
(2001) ***Gene Therapy***, 8:1555-1561.

Membrane immunoglobulins are stabilized by inter-chain disulphide bonds occurring within the extracellular membrane-proximal domain.
Marco Bestagno, Luca Vangelista, Paola Mandiola, Shibani Mukherjee, Jorge Sepúlveda and Oscar R. Burrone.
(2001) ***Biochemistry***, 40:10686-10692.

Genetic vaccination for the immunotherapy of B-cell malignancies
F. Benvenuti and O. R. Burrone
(2002) ***Curr. Gene Therapy,*** 2:235-242.

A minimal receptor–Ig chimera of human FcεRI α-chain efficiently binds secretory and membrane IgE.
L. Vangelista, M. Cesco Gaspere, R. Lorenzi and O. R. Burrone
(2002) ***Protein Engineering***, 15:51-57.

Rotavirus NSP5: Mapping phosphorylation sites and kinase activation and viroplasm localisation domains.
C. Eichwald, F. Vascotto, E. Fabbretti and O.R. Burrone
(2002) ***J. Virol.***, 76:3461-3470.

Anti-Idiotypic DNA vaccines for B-cell lymphoma therapy.
F. Benvenuti, M. Cesco-Gaspere and O.R. Burrone.
(2002), ***Frontiers in Bioscience,*** 7:d228-234, http://bioscience.org.

Selective targeting of tumoral vasculature: comparison of different formats of an antibody (L19) to the ED-B domain of Fibronectin.
L. Borsi ,E. Abalza, M. Bestagno, P. Castellani, B. Carnemolla, A. Biro, A. Leprini, J. Sepulveda, O. R. Burrone, D. Neri and L. Zardi.
(2002) ***Int. J. Cancer,*** 102:75–85.

Efficient folding of the FcεRI α-chain membrane-proximal domain D2 depends on the presence of the N-terminal domain D1
L. Vangelista, M. Cesco-Gaspere, D. Lamba and O.R. Burrone
(2002) ***J.Mol.Biol.,*** 322:815-825.

Molecular cloning and characterisation of and inhibitory anti-cathepsin B antibody and its expression in Chinese Hamster Ovary cells.
X. Fan, N. Kopitar-Jerala, A. Premzl, M. Bestagno, O.R. Burrone and J. Kos.
(2002) ***Biol. Chem.,*** 383:1817-1820.

Evidence of CXC, CC and C chemokines production by lymphatic endothelial cells.
S Mancardi, E Vecile, N Dusetti, E Calvo, G Stanta, O.R. Burrone and A Dobrina·
(2003) ***Immunology***, 108:523-530.

Recombinant antibodies in the immunotherapy of neuroblastoma: Perspectives of new developments.
Bestagno M., Occhino M., Corrias M.V., Burrone O.R., Pistoia V.
(2003) ***Cancer Letters***, 197:193-198.

Binders based on dimerised immunoglobulins V_H domains.
Sepúlveda J, Jin H, Sblattero D, Bradbury A and Burrone O.R.
(2003) ***J. Mol. Biol.,*** 333: 355-365

Selection and characterisation of binders based on homo-dimerisation of immunoglobulin V_H domains.
Hulin Jin, Jorge Sepúlveda and Oscar R. Burrone.
(2003) ***FEBS Letters,*** 554:323-329

Characterisation of rotavirus NSP2/NSP5 interaction and dynamics of viroplasm formation.
Catherine Eichwald, José Francisco Rodriguez and Oscar R. Burrone
(2004) ***J. Gen. Virol.,*** 85:625-634

Generation and Characterisation of dimeric small immunoproteins specific for neuroblastoma associated antigen GD2.
Marzia Occhino, Lizzia Raffaghello, Oscar R. Burrone, Claudio Gambini, Vito Pistoia, Maria Valeria Corrias and Marco Bestagno.

(2004) ***Int. J. Mol. Med.,*** 14:383-388.

Effect of intrabodies specific for rotavirus NSP5 during the viral replicative cycle.
Fulvia Vascotto, Michela Campagna, Michela Visintin, Antonino Cattaneo and Oscar R. Burrone.
(2004) ***J. Gen. Virol.,*** 85:3285-3290.

Specific recognition of a dsDNA sequence motif by an immunoglobulin V_H homo-dimer.
Hulin Jin, Jorge Sepúlveda and Oscar R. Burrone.
(2004) ***Protein Science,*** 13:3222-3229.

Uncoupling substrate and activation functions of rotavirus NSP5: phosphorylation of Ser67 by CK1 is essential for hyperphosphorylation
Catherine Eichwald, Germaine Jacob, Bartosz Muszynski, Jorge E. Allende and Oscar R. Burrone
(2004) ***Proc. Natl. Acad. Sci. USA,*** 101:16304–16309

RNA interference of rotavirus segment 11 mRNA reveals the essential role of NSP5 in the virus replicative cycle
M. Campagna, C. Eichwald, F. Vascotto and O.R. Burrone
(2005) ***J. Gen. Virol.*** 86:1483-1489.

BCL1 lymphoma protection induced by idiotype DNA vaccination is entirely dependent on anti-idiotypic antibodies.
Michela Cesco-Gaspere, Federica Benvenuti and Oscar R. Burrone.
(2005) ***Cancer Immunol. Immunother.,*** 54:351-358.

Membrane IgE binds and activate FcεRI in an antigen-independent manner.
Vangelista, L.,, Soprana, E., Cesco-Gaspere, M., Mandiola-Sáenz, P., Di Lullo G., Fucci, R.N., Codazzi, F., Palini A., Paganelli, G., Burrone, O.R., Siccardi, A.G.
(2005) ***J. Immunol.***, 174:5602-5611.

Design and selection of a *de-novo* produced intrabody library for the non–structural protein NSP5 of rotavirus.
Vascotto, F., Visintin, M., Cattaneo A., Burrone, O.R.
(2005) ***J. Immunol. Meth.***, 301:31-40

Rotavirus VP7 antigen produced by *Lactococcus lactis* induces neutralising antibodies in mice.
Perez, C.A., Eichwald, C.,, Burrone, O.R., de Mendoza, D.

(2005) ***J. Appl. Microbiol.*** 99:1158-1164

Fusion of Tags induces spurious phosphorylation of rotavirus NSP5
Campagna, M., Burrone, O.R.
(2006) ***J. Virol.*** 80:8283-8285

An antibody derivative expressed from viral vectors passively immunises pigs against *Transmissible Gastroenteritis Virus* infection when supplied orally in crude plant extracts.
Monger′ W. Alamillo, J.M., Solá. I., Perrin, Y., Bestagno, M., Burrone, OR., Sabella, P., Plana-Duran, J., Enjuanes, L., Garcia, JA., Lomonossoff, GP.
(2006) ***Plant Biotechnology Journal,*** 4:623-631

The Extracellular Membrane Proximal Domain of human membrane IgE controls apoptotic signalling of the B Cell Receptor in the mature cell line A20.
Poggianella, M., Bestagno, M., Burrone, O.R.
(2006) ***J. Immunol.*** 177:3597-3605

Use of virus vectors for the expression in plants of active full-length and single chain anti-coronavirus antibodies.
Alamillo, J.M., Monger′ W., Solá. I., Garcia, B., Perrin, Y., Bestagno, M., Burrone, OR., Plana-Duran, J., Enjuanes, L., Lomonossoff, GP., Garcia, JA.
(2006) ***Biotechnology Journal*** 1:1103-1111

Recombinant dimeric small immune proteins (SIPs) efficiently neutralise *Transmissible Gastroenteritis Virus* infectivity *in vitro* and confer passive immunity *in vivo*.
Bestagno, M., Sola, I., Dallegno, E., Sabella, P., Poggianella, M.,
Plana-Durán, J., Enjuanes, L., Burrone, O.R.
(2007) ***J. Gen. Virol.*** 88:187-195

Interaction of the rotavirus polymerase VP1 with non-structural protein NSP5 is stronger than with NSP2
Arnoldi, F., Campagna, M., Eichwald, C., Desselberger, U., Burrone, O.R.
(2007) ***J. Virol.*** 81: 2128–2137

Gangliosides, Ab1 and Ab2 antibodies. III. The idiotype of anti-ganglioside mAb P3 is immunogenic in a T cell-dependent manner.

López-Requena, A., Bestagno, M., Mateo de Acosta, C., Cesco-Gaspere, M., Vázquez, A.M., Pérez, R., Burrone, O.R. (2007) ***Mol. Immunol.*** 44:2915-2922

Gangliosides, Ab1 and Ab2 antibodies. IV. Dominance of VH domain in the induction of anti-idiotypic antibodies by gene gun immunisation.
López-Requena, A., Mateo de Acosta, Bestagno, M., C., Vázquez, A.M., Pérez, R., Burrone, O.R.
(2007) ***Mol. Immunol.*** 44:3070-3075

Impaired hyperphosphorylation of rotavirus NSP5 in cells depleted of CK1-α is associated with the formation of viroplasms with altered morphology and a moderate decrease in virus replication.
Campagna, M., Budini, M., Arnoldi, F., Desselberger, U., Allende, J.E., Burrone, O.R.
(2007) ***J Gen. Virol***. 88:2800-2810

Construction of miniantibodies for the in vivo study of human autoimmune diseases in animal models.
Di Niro R., Ziller, F., Florian, F., Crovella, S., Stebel, M., Bestagno, M., Burrone, O.R. Bradbury, A.R.M., Secco, P., Marzari, R., Sblattero, D.
(2007) ***BMC Biotechnology*** 7:46

Selection of an antibody library identifies a pathway to induce immunity by targeting CD36 on steady state CD8α^+ dendritic cells.
Tagliani E., Guermonprez P., Sepúlveda J., Lopez Bravo M., Ardavin C., Amigorena S., Benvenuti, F., Burrone O.R.
(2008) ***J. Immunol.***, 180:3201-3209

In vivo site-specific biotinylation of proteins within the secretory pathway using a single vector system.
Predonzani, A., Arnoldi, F., López-Requena, A., Burrone, O.R.
(2008) ***BMC Biotechnology,*** 8:41

Boosting anti-idiotype immune response with recombinant AAV enhances tumour protection induced by Gene Gun vaccination.
Cesco-Gaspere, M., Zentilin, L., Giacca, M., Burrone, O.R.
(2008) ***Sc. J. Immunol.*** 68:58-66

Expression of Wiskott-Aldrich syndrome protein in dendritic cells regulates synapse formation and activation of naive CD8+ T cells.

Pulecio J., Tagliani, Scholer, A., E., Prete F., Fetler, L., Burrone, O.R., Benvenuti, F.
(2008) ***J.Immunol***, 181:1135-1142

Anti-Idiotypic Antibodies and “Tumor-Only” Antigens: An Update
López-Requena, A., Burrone, OR.
(2009) ***The Open Immunology Journal***, 2:1-8

Role of viral non-structural proteins in rotavirus replication
Arnoldi, F., Burrone, OR.
(2009) ***Future Virology***, 4:185-197

CD57+ T lymphocytes and functional immune deficiency.
Focosi, D., Bestagno, M., Burrone, O., Petrini, M.
(2010) **J. Leukoc. Biol.** 87:107-116

Rotavirus NSP5 orchestrates recruitment of viroplasmic proteins.
Contin R., Arnoldi, F., Campagna, M., Burrone O.R.
(2010) ***J Gen. Virol.*** 91:1782-1793

Cdc42-mediated MTOC polarization in dendritic cells controls targeted delivery of cytokines at the immune synapse.
Pulecio J., Petrovic, J., Prete, F., Chiaruttini, G., Lennon-Dumenil A.M., Desdouets C., Gasman, S., Burrone, O.R. and Benvenuti, F.
(2010) ***J. Exp. Med.*** 207:2719-2732

Rotavirus replication requires a functional proteasome for effective assembly of viroplasms.
Contin, R., Arnoldi, F Mano, M. and Burrone, O.R.
(2011) ***J. Virol.*** 85: 2781–2792.

Efficient Detection of Proteins Retro-Translocated from the ER to the Cytosol by In Vivo Biotinylation.
Petris G, Vecchi L, Bestagno M, Burrone OR
(2011) ***PlosOne*** 6(8): e23712

Production of *in vivo* Biotinylated Rotavirus Particles.
De Lorenzo G., Eichwald C., Schraner E.M., Nicolin V., Bortul R.,
Burrone O.R. and Arnoldi F.
(2012) *J Gen. Virol.,* 93:1474-82

Selective Targeting of Proteins within the Secretory Pathway for Endoplasmic Reticulum-Associated Degradation
Vecchi L., Petris G., Bestagno M., Burrone O.R.
(2012) *J. Biol. Chem.* 287:20007-15

Rotavirus Viroplasm Fusion and Perinuclear Localization are Dynamic Processes Requiring Stabilized Microtubules
Eichwald C., Arnoldi F., Laimbacher A.S., Schraner E.M., Fraefel C., Wild P., Burrone O.R., Ackermann M.
(2012) *PlosONE,* 7(10):e47947

Idiotypes as immunogens: facing the challenge of inducing strong immune responses against the variable region of immunoglobulins.
López Requena A., Burrone O.R., Cesco-Gaspere M.
(2012) *Frontiers in Oncology,* doi: 10.3389/fonc.2012.00159

Rotavirus Viroplasm Proteins Interact with the Cellular SUMOylation System: Implications for Viroplasm-Like Structures Formation.
Campagna M., Marcos-Villar L., Arnoldo F., de la Cruz-Herrera C.F., Gallego P., González-Santamaría J., González D., Lopitz-Otsoa F., Rodríguez M.S., Burrone, O.R., Rivas, C.
(2013) *J Virol.,* 87:807-817

Retro-translocation of proteins from the ER to the cytosol

Oscar R. Burrone
International Centre for Genetic Engineering and Biotechnology, Trieste, Italy

The cellular quality control of proteins synthesised within the secretory pathway initiates in the ER, where the folding state is monitored. Misfolded molecules, however, are degraded in the cytosol by the 26S proteasome. Therefore molecules targeted to degradation must exit the ER in a process known as retro-translocation. We have recently developed a novel methodology to monitor retro-translcoation taking advantage of the E. coli derived biotin-ligase (BirA) expressed in the cytosol of mammalian cells to specifically biotinylate in vivo proteins dislocated to the cytosol. We have applied this technique to investigate the mechanism of retro-translocation, using different model proteins.