

MASUCCI MARIA GRAZIA

Nata il 15 gennaio 1953, è ricercatrice e professoressa di Virologia presso il Dipartimento di Biologia cellulare e molecolare del Karolinska Institutet di Stoccolma dal 1997.

In seguito agli studi universitari in medicina presso l'Università di Ferrara, dove si è laureata nel 1977 specializzandosi in oncologia sperimentale, ha iniziato la sua attività di ricerca presso il Dipartimento di Microbiologia sempre a Ferrara, trasferendosi in seguito al Karolinska Institute dove ha presentato nel 1985 la tesi di dottorato sul virus di Epstein-Barr.

Dal 1987 professoressa associata di Biologia del tumore e dal 1997 professoressa di Virologia presso il Karolinska Institute.

La sua ricerca verte sul legame tra infezioni virali, il cancro e il sistema immunitario. Dal 2006, è membro dell'Accademia Reale Svedese delle Scienze.

Scientific profile

My work investigates the molecular mechanisms of viral pathogenesis using as model Epstein-Barr virus (EBV), an oncogenic lymphotropic human herpesvirus. EBV infects the vast majority of adults worldwide and is probably the most widespread virus in humans. Primary infection occurs in childhood and is clinically silent but leads to the establishment of a carrier state that may give rise to important pathologies later in life. The best-studied consequence of EBV infection is the association of the virus with malignancies of lymphoid and epithelial cell origin including Burkitt's lymphoma, Nasopharyngeal carcinoma and a subset of Hodgkin's lymphoma and gastric carcinomas. A rough estimate implicates EBV in the pathogens of approximately 1% of all human cancers with important difference in the geographic- and age-distribution of the different types, which is likely to be associated to the requirement for genetic, environmental and age-related co-factors. Recent evidence suggests that, in addition to its relatively well-understood oncogenic properties, EBV infection plays an important role in the pathogenesis of a variety of chronic degenerative and autoimmune diseases that affect the elderly populations. In particular, epidemiological and serological data indicate that the normally watertight immunological control that allows the life-long persistence of the virus in healthy carriers is altered in patients suffering from systemic lupus erythematosus (SLE), multiple sclerosis (MS) and rheumatoid arthritis (RH) that often affect elderly women. The precise role of the virus in the pathogenesis of these diseases is still poorly understood but a common feature is the presence of altered antibody titers against viral antigens and the secretion of high amounts of viral DNA and infectious virus, which points to impaired control of virus replication as a possible cause of chronic inflammation. Furthermore, immune senescence in the elderly is associated with both reactive and neoplastic EBV driven lymphoproliferative disease, including EBV-positive large B-cell lymphoma. My scientific contributions have addressed the immunological control of viral infection, the mechanisms of immune escape and the molecular mechanisms by which the virus reprograms the host cell in order to achieve efficient replication and promote malignant transformation. We have identified antigenic epitopes and characterized cytotoxic T lymphocyte (CTL) responses in terms of epitope selection and T-cell receptor repertoire. Monitoring of virus load and expansion of EBV specific CTLs were used to characterize immune responses in Hodgkin's Disease (HD) and Nasopharyngeal carcinoma (NPC) patients and adoptive CTL transfer was tested for the prophylaxis of EBV lymphomas in bone marrow transplant recipients. The demonstration that the EBV nuclear antigen EBNA-1 escapes CTL recognition led to the identification of the glycine-alanine repeat (GAR) as the first example of a protein domain that blocks proteasomal processing. Work on viral pathogenesis addresses the role of viral proteins and non-coding RNAs in the reprogramming of infected cells. We have shown that the EBV nuclear antigen EBNA1 causes non-clonal chromosomal aberrations in EBV associated malignancies, which correlates with the induction of DNA damage and telomere dysfunction via production of reactive oxygen species (ROS). EBNA1 promotes an epigenetic reprogramming of the infected cells by mimicking the activity of cellular high mobility group-A proteins that induce DNA decompaction and allow a broad rearrangement of cellular transcription. Ongoing work aims to characterize the cellular and viral factors that promote a global remodeling of the cellular

environment during virus replication. This work focuses on the identification of regulatory interactions that may offer new targets for therapeutic intervention with the ultimate goals to achieve a more effective control of virus replication. This effort is particularly relevant in the context of the chronic inflammatory diseases associated with virus infection and could also play an important role in decreasing the risk of malignancies in the elderly.

CURRICULUM VITAE

A. EDUCATION

1988 Lecturer (Docent) of Tumor Biology with specialization in Tumor Immunology

1985 PhD in Tumor Immunology, Karolinska Institute, Stockholm, Sweden.

1980 Specialization in Experimental Oncology, University of Ferrara, Italy

1977 MD degree, University of Ferrara, Italy.

B. APPOINTMENTS

2002-2003 Visiting Professor Department of Cell Biology, Harvard Medical School, Boston, MA

1997 – Professor of Virology, Karolinska Institutet, Stockholm, Sweden

1992-1997 Research fellow of the Swedish Cancer Society

1978-1992 Research associate at the Department of Tumor Biology, Karolinska Institutet

C. FELLOWSHIPS, AWARDS AND PRIZES

Concern Foundation for Cancer Research, California, USA – Young investigator award (1991-1993); Swedish Foundation for Strategic Research – Senior Investigator award in Biomedical Sciences (1998-2003); Swedish Research Council – Award for excellence in medical research (2004-2005); Swedish Medical association, Jubilee prize 2005; Karolinska Institutet – Distinguished Professor Award (2010-2014); Swedish Royal Academy of Sciences – Hilda and Alfred Eriksson prize (2013)

D. MEMBERSHIPS

Italian Society of Immunology (1982); Scandinavian Society of Immunology (1984); Swedish Medical Association (1985); EBV association (1988); Italian Virology Society (honorary member, 2000); Nobel Assembly for physiology and medicine (2003); Nobel Committee (2003, 2005, 2006, 2007); EMBO member (2005), Swedish Royal Academy of Sciences (2006)