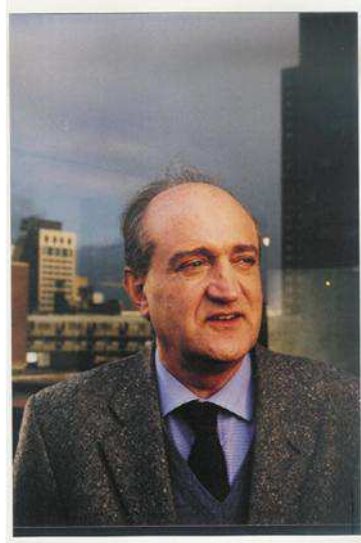


Prof. Pier Mario Biava



The Code which organizes life and its different functions: reprogramming cells.

Medicine is moving towards the change of scientific paradigm already undergone by physics. This change will shift the biological-mechanical approach into a systemic vision and approach in which the living being participates to an information network at quantum level that has to be fine-tuned in a physiological way.

The premises of a paradigm changing research

In an article published in 1988 in *Cancer Letter* and written together with my collaborators of the Institute of Labor Medicine of the University of Trieste and with researchers from the National Tumor Institute in Milan, we described right from the premise how our work was based on the hypothesis that tumors were reversible pathologies. In fact, scientific observations demonstrated that factors of the embryonic microambience were able to reprogram cancer cells, bringing them back to normal behaviour. After this first work, my studies continued in collaboration with various Universities: La Sapienza University of Rome, the Universities of Pisa and Bologna as well as foreign Universities (with Professor Klavins of Cornell University, New York, and Professor Ablijn of the University of Arizona. Professor Ablijn is famous throughout the world because he discovered PSA, the first marker of prostate cancer. This research work was carried on for quite a long time without waking an interest among the scientific community because most researchers and oncologists concentrated their attention and research work on mapping the DNA and isolating single genes that could be important in causing tumors. In the meantime, however, our research work, conducted during a sufficiently long period, had permitted to single out the different molecular mechanisms by which the differentiation factors of normal stem cells, taken from Zebrafish embryos (this embryo had been chosen because it is the best studied model of embryonic differentiation) were able to differentiate cancer cells or bring them to a programmed cellular death. Moreover, the substances constituting such factors had been isolated and the

single molecules that entered the composition of the various differentiating networks had been identified using gas chromatography mass spectrometry.

The systematic study of the life organizing code: the epigenetic code.

From our studies we had understood that what we were studying was the code which is now defined as "epigenetic", i.e. the code entirely present in the embryo, when life is forming, whereas in the adult individual it is present only very partially in single organs. At the beginning of this century, after the termination of the sequencing of all DNA genes, when it became clear that the genetic code alone – upon which all hopes to change the destiny of cells had been concentrated – could not do anything, the scientific community started to focus their attention elsewhere. In fact, researchers widened their view from the genetic code to comprise also the epigenetic code. At that point, my research work had already much advanced and permitted to understand that the specific and selective use of the epigenetic code could determine the destiny of both normal and pathological stem cells. The epigenetic code is in fact a proper regulator, able to activate or inactivate the different genes, targets of our intervention.

The different functions and the incredible regulating activities of the code of life.

Now, a fraction of the epigenetic code has been identified, a fraction that **for the first time ever** proved its natural ability, without gene manipulation, to maintain the stem cell genes **that impede cell aging** (they are the same genes introduced artificially by means of a retrovirus into a differentiated cell by Shinya Yamanaka who, in 2012 won the Nobel prize for this experiment. Because of the manipulations it has undergone, however, the differentiated cell cannot be used safely. In our research work, **the cells stay young without manipulation**, due a **physiological regulation** of the stem cell genes. Furthermore it was confirmed that a different part of the epigenetic code is on the contrary able **to slow down cellular multiplication through differentiation of the cells or inducing a programmed cellular death (this had already been observed in the altered multiplication processes that occur in pathologies like cancer and psoriasis)**. At last, it has been demonstrated that a **redundance of factors of the epigenetic code are able to significantly impede degeneration of nerve cells** (this happens because initially the redundancy of factors, actually of all the factors present from the beginning to the end of the differentiation process, at first expands the number of stem cells and then differentiates them into the specific tissue). Studies are still under way to understand ever better how the epigenetic code, which is at the proper origin of life, works in repairing tissues, so that it can be used in **regenerative medicine**, in particular for the pathologies where stem cell transplantations are needed. The mentioned epigenetic regulators can in fact **potentiate the positive effects brought by stem cell transplantations and may in the future work as a substitute of the transplants** if we consider that the positive effects of stem cell transplantations are not due to the transplanted cells but to the factors produced by them. Such factors are those taken from the Zebrafish embryo. As said before, they are proteins and nucleic acids with regulatory properties and it has been demonstrated that they are the same in the human species.

A radical shift of the scientific paradigm.

What appeared clearly at last, is that life organizes itself on the basis of **information programs which deliver, just like software applications, precise instruction packages. These packages are inseparable units which will not be used, if fragmented**. On the other hand, the most recent and modern research has demonstrated how these regulatory factors are transferred to the cells as different information packages, contained in vesicles called **exosomes**, which, based on their information content, i.e. the specific regulatory factors, target specific cells. In other words, **the**

information transported also contains the destination where it has to be transferred to. The research work presented brings a different thinking and a shift of the scientific paradigm with it. The human being and the living being are no longer seen as mechanical aggregates, whose behaviour can be modified in artificial ways, but, in a systemic approach, as information networks that have to be fine-tuned in a physiological way.

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EUROPASS CURRICULUM VITAE



PERSONAL INFORMATION

First name / Surname Pier Mario Biava

E-mail **biava@tiscali.it**

Nationality Italian

Date of birth March, 7th, 1944

WORK EXPERIENCE

- Date *January 1, 1970 to October 6, 1970*
 - Name and address of employer Psychiatric service – Provincial Authority of Reggio Emilia
 - Type of business or sector *Healthcare*
 - Occupation or position held Assistant physician
 - Main activities and responsibilities
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- Date *October 7 to April 10, 1973*
 - Name and address of employer Occupational medicine service - Provincial Authority of Reggio Emilia
 - Type of business or sector *Healthcare*
 - Occupation or position held Executive
 - Main activities and responsibilities Organization work for the Occupational medicine and Environmental hygiene services of the Provincial authority of Reggio Emilia, involving surveys in different areas.
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- Date *April 12, 1973 to May 31, 1977*
 - Name and address of employer Occupational Medicine Institute - University of Trieste
 - Type of business or sector *Healthcare*
 - Occupation or position held Assistant
 - Main activities and responsibilities
-
- Date *June 1, 1977 to November 1, 1984*
 - Name and address of employer Occupational Medicine Institute - University of Trieste
 - Type of business or sector *Healthcare*
 - Occupation or position held Vice-Director
 - Main activities and responsibilities
-
- Date *November 2, 1984 to 2007*
 - Name and address of employer Occupational Therapy Hospital Service - Sesto San Giovanni
 - Type of business or sector *Healthcare*
 - Occupation or position held Director physician and Director of Research on Stem Cells and Cancer
 - Main activities and responsibilities Between 1986 and February of 1991 I General Director at the Sesto San Giovanni hospital.

- Date 2007 to date
- Name and address of employer Occupational medicine - Sesto San Giovanni at Gruppo MultiMedica Holding SpA
 - Type of business or sector Healthcare
 - Occupation or position held Consultant
- Main activities and responsibilities Occupational physician and researcher

EDUCATION AND TRAINING

- Date 1969
- Name and type of organization providing education and training Degree in Medicine and Surgery at the University of Pavia – Final grade: 110/110 with honors
- Principal subjects/occupational skills covered
 - Title of qualification awarded University degree
- Level in national or international classifications

- Date 1973
- Name and type of organization providing education and training Major in Occupational medicine at the University of Padua (Final grade 70/70)
- Principal subjects/occupational skills covered
 - Title of qualification awarded Major
- Level in national or international classification

- Date 1977
- Name and type of organization providing education and training Specialty in Hygiene and preventive medicine – Public Health at the University of Trieste 70/70 with honors
- Principal subjects/occupational skills covered
 - Title of qualification awarded Specialty
- Level in national or international classification

- Date 1980
- Name and type of organization providing education and training Certificate of attendance to the 1st National Epidemiology Course held by the National Healthcare Institute n Rome
- Principal subjects/occupational skills covered
 - Title of qualification awarded Certificate of attendance
- Level in national or international classification

- Date 1979 to 2002
- Name and type of organization providing education and training Professor at the Occupational Medicine post-graduated school at the University of Trieste
- Principal subjects/occupational skills covered Medicine
 - Title of qualification awarded Professor
- Level in national or international classification

- Date 1981

- Name and type of organization providing education and training National head physician certificate - 100/100
- Principal subjects/occupational skills covered
- Title of qualification awarded Head physician certificate
- Level in national or international classification

TEACHING

- Date 1981, 1982, 1983, 1984
- Name and type of organization and training Professor of "Industrial technology" and "Professional disease epidemiology"
- Principal subjects/occupational skills covered Healthcare
- Title of qualification awarded Professor
- Level in national or international classification
- Date 1984 to 2002
- Name and type of organization and training Professor at the University of Trieste: "Healthcare service organization"
- Principal subjects/occupational skills covered Medicine
- Title of qualification awarded Professor
- Level in national or international classification
- Date 2003 to 2004
- Name and type of organization and training Professor at the "La Sapienza" University - Rome
- Principal subjects/occupational skills covered Healthcare
- Title of qualification awarded Professor
- Level in national or international classification

PERSONAL SKILLS AND COMPETENCES

I am the author of **approximately 100 papers** on prevention, health protection and basic and applied biomedical research in oncology..I was **Guest Editor** of a special issue about **"Reprogramming of Normal and Cancer Stem Cells" published by Current Pharmaceutical Biotechnology (Vol 12 N2 - 2011)**. In this field of research I coined a new control approach to tumor growth based on the use of stem cell differentiation factors collected from oviparous embryos (Zebrafish) in different stages of cell differentiation. Moreover, I discovered a low molecular weight protein fraction (5kD) in pregnant uterus mucosa that blocks tumor growth in several human carcinomas in vitro (glioblastoma, melanoma, breast cancer, kidney adenocarcinoma, lymphoblastic leukemia). This fraction was given the name of "Life Protecting Factor"

I am author of a **book entitled "L'aggressione nascosta. Limiti Sanitari di Esposizione ai Rischi". Feltrinelli Editore 1982.** I edited the book **"Complessità e biologia" published in 2002 by Bruno Mondadori.** I am co-author of the book **"Il cancro fra mente e corpo" published by Riza in 2004.** I am author of the book **"Il Cancro e la Ricerca del Senso Perduto" published by Springer. (2008)** Author of **Cancer and the Search for Lost Meaning published by North Atlantic Book (english edition 2009),** author of **" Revolution in der Krebs Therapie (German Edition) published by Verlag Vianova (2010)** and author of **Il Senso Ritrovato (with Ervin Laszlo) publishing by Springer (2012).**

MOTHER TONGUE Italian

OTHER LANGUAGES

	English
•Reading	Good
•Writing	Good
•Spoken production	Good
	French
•Reading	Good
•Writing	Good
•Spoken production	Fair

PERSONAL SKILLS AND COMPETENCES

SPEAKER IN MANY INTERNATIONAL SYMPOSIA AND SEMINARS. HE WAS PRESIDENT OF THE EUROPEAN INSTITUTE FOR COMPLEXITY STUDIES, A NON-PROFIT ORGANIZATION THAT SPONSORED MANY STUDIES OF CLEAR INTERNATIONAL STATURE. THE INSTITUTE IS IN CONTACT WITH THE EQUIVALENT IN SANTA FE, WITH WHICH IT ORGANIZED MANY SEMINARS: THE MOST RECENT SAW THE PARTICIPATION OF MURRAY GELL-MANN, NOBEL PRIZE FOR PHYSICS THANKS TO HIS QUARK THEORY. MOREOVER, I WAS PRESIDENT OF "FONDAZIONE PER LA RICERCA DELLE TERAPIE BIOLOGICHE DEL CANCRO". BOTH IN MY MEDICAL ACTIVITY IN HOSPITALS AND IN MY PROFESSIONAL RELATION WITH COLLEAGUES AT INTERNATIONAL LEVEL I HAVE ALWAYS HELD PRIMARY ROLES AND POSITIONS, WHILE BEING ABLE TO INVOLVE ALL STAKEHOLDERS IN A TEAMWORK-ORIENTED APPROACH.

TECHNICAL SKILLS AND COMPETENCES

Both in my professional and voluntary work (I have been member of the Board of Directors of Fondazione della Banca UniCredit, a non-profit foundation, promoting health protection and improvement of social conditions in several areas of the world) I have always been an efficient organizer, drafting aid and rescue plans that were always appreciated and approved. I perform my tasks as occupational physician and oncology researcher with great dedication and competence.

ARTISTIC SKILLS AND COMPETENCES

A skilled writer and author of several books

OTHER SKILLS AND COMPETENCES

Not previously reported

Member of the editorial council in the following journals:
 "Epidemiologia e Prevenzione"
 "Journal of Tumor Marker Oncology"
 I was Vice-President of the International Academy of Tumor Marker Oncology"

DRIVING LICENSE

ADDITIONAL INFORMATION

ANNEXES

The undersigned is aware of the legal consequences in case of misrepresentation, false statements in documents and use of false documents under Article 26 of Law 15/68, the Criminal Code and a set of Special Laws. Moreover, the undersigned authorizes the processing of his data under the provisions of Law 196/03.

Place and date
 Milano, September, 2012

NAME AND SURNAME (SIGNATURE)
