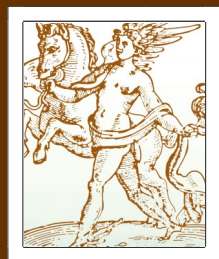


STEM CELLS, CANCER, IMMUNOLOGY AND AGING

HIGHLIGHTS



Fondazione
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February 12-14, 2015
Genoa

STEM CELLS, CANCER, IMMUNOLOGY AND AGING

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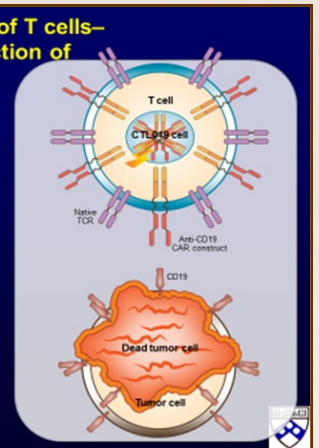
HIGHLIGHTS

Chimeric Antigen Receptors (CAR) T Cell Therapy” - Present and future

By using modern gene transfer technologies it is possible to stably induce the expression of the Chimeric Antigen Receptors on T cells, which, being enriched in this way with new antigenic specificities, can thus be directed against any cancer cells that express their CD19 surface antigen. This cell line, called CTL019, keeps the cytotoxic potential of the T cells intact, killing the cancer cells in an antigen-dependent manner. These cells also keep the antibody “memory” alive that acts against the specific antigens found on the cancer cells. This therapy is extremely effective when applied in patients with acute lymphatic leukaemia, as demonstrated by the data presented by Prof. Barrett.

Redirecting the Specificity of T cells– Proposed Mechanism of Action of CTL019 cells

- Gene transfer technology is used to stably express CARs on T cells, conferring novel antigen specificity^{1,2}
- CTL019 cells can thus be directed against any tumor cell that expresses the CD19 surface antigen
- CTL019 therapy takes advantage of the cytotoxic potential of T cells thereby killing tumor cells in an antigen-dependent manner^{1,3}
- Persistent CTL019 cells consist of both effector (cytotoxic) and central memory T cells³



1. Mitsuoka M, et al. Mol Ther. 2009;17:1453-1464.
2. Hoshizumi A, et al. J Immunother. 2009;32:169-180.
3. Kalos M, et al. Sci Transl Med. 2011;3:56ra73.



David Barrett
Perelman School
of Medicine
University
of Pennsylvania
Philadelphia (USA)

What is the life expectancy today of a patient with acute lymphatic leukaemia that has relapsed?

For more in-depth information click on the following link: www.fondazione-menarini.it/..... and after having logged in, access the multimedia material.

New strategies for Haematopoietic stem cell transplants: what's new ?...

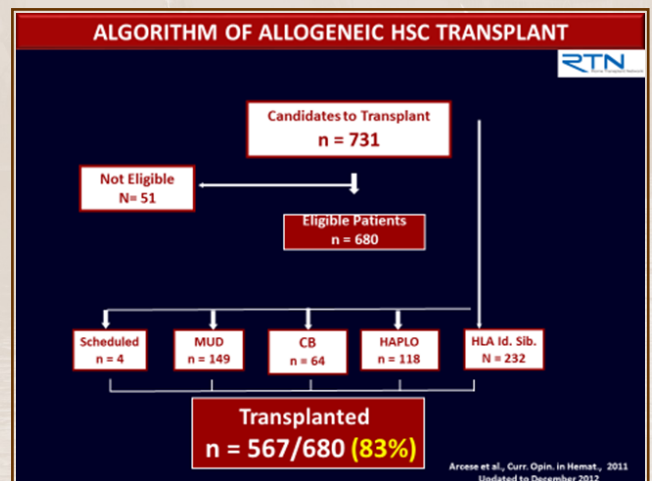
Recent literature has shown that nearly 90% patients who are candidates for allogeneic transplants of haematopoietic stem cells can be recipients of transplants. This has been possible thanks to the higher number of donors than in the past. There has also been a dramatic drop in mortality directly related to the transplant, even in high-risk populations such as patients suffering from refractory anaemia with an excess of blast cells, one of the most severe forms of the myelodysplastic syndrome.

What's behind this success?

For more in-depth information click on the following link: www.fondazione-menarini.it/..... and after having logged in, access the multimedia material.



Andrea Bacigalupo
IRCCS AOU
San Martino
Genoa (Italy)



Arceus et al., Curr. Opin. in Hemat., 2011
Updated to December 2012

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Francesco Frassoni
Istituto Giannina Gaslini
Genoa (Italy)

Has the promise become reality ?!

Leukaemia patients who previously had little chance of survival with the current therapies can now take advantage of an innovative treatment such as that implemented via the application of the “CAR T cells”. But what are the minimum requirements for enabling a qualified centre to produce CAR T cells? What investments are necessary? What is the minimum necessary staffing? What are the “regulatory” requirements for also authorising this effective and innovative therapy in Europe? What funds are necessary for such an investment?

CAR T cells

The promise is a reality

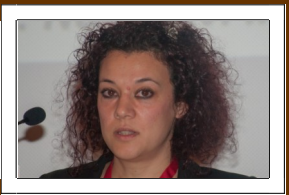
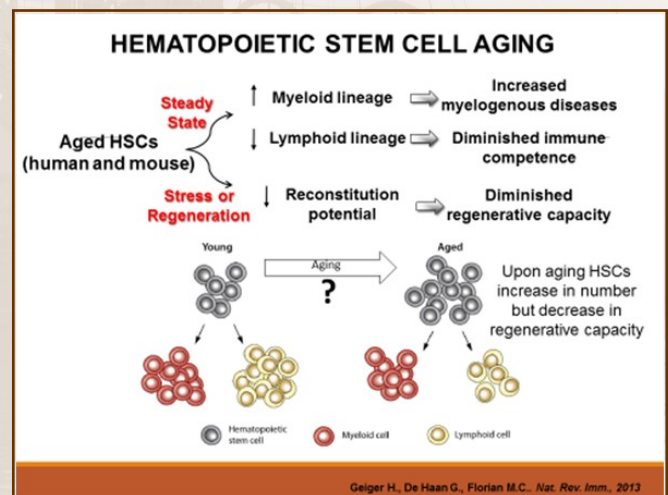
The achievements and developments
of CAR-T cells in Leukemia

To find the answers to these and other important questions posed by Prof. Frassoni:

Click on the following link: www.fondazione-menarini.it/..... and after having logged in, access the multimedia material.

Aging and regeneration of the haematopoietic stem cells: is this a feasible situation?

The aging of the population is a phenomenon that involves not only countries with high economic standards, in fact, it is estimated that by 2050 there will be a global increase in the percentage of elderly people compared to the total population throughout the world. What will be the consequences of this aging population, and will it also affect the stem cells? As we get older, our stem cells are subjected to the phenomena linked to aging. In particular, despite maintaining a good morphological profile, our haematopoietic stems cells lose part of their regenerative capacity, and this phenomenon is more evident at the level of the immune system which loses part of its efficiency over time. This is one of the causes of the increased incidence of leukaemia linked to the aging processes. What is the mechanism that drives these processes towards aging? The presence of high quantities of a protein called Cdc 42 in mice but also in the human organism, seems to be a decisive factor in the genesis of the aging processes, as demonstrated by Prof. Florian in her talk.



Carolina Florian
Institute of Molecular
Medicine and
Stem cell Aging
University of Ulm
(Germany)

Can these processes be reversible? Is it possible to somehow reduce the presence of this protein in living organisms?

For more in-depth information click on the following link: www.fondazione-menarini.it/..... and after having logged in, access the multimedia material.

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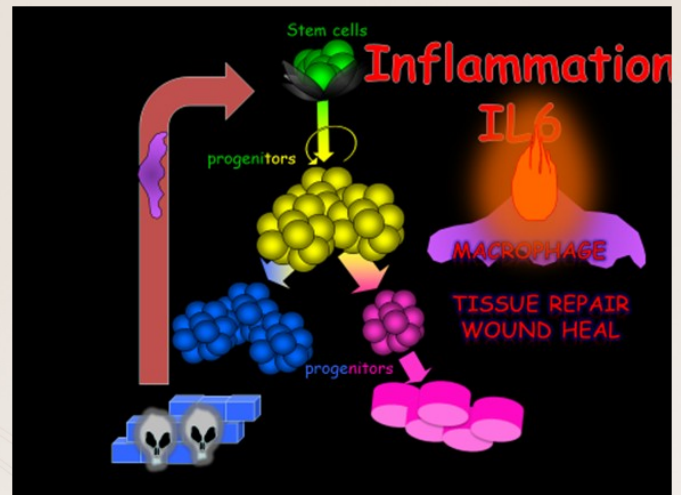
HIGHLIGHTS



Massimiliano Bonafè
Dipartimento di
Medicina Specialistica,
Diagnostica e
Sperimentale,
University of Bologna
(Italy)

Is there a common biological line between cancer and aging?

It has been discovered that the “Beta catenin”, the central point in the Wnt/Beta-catenin signalling pathway, carries out numerous essential functions for cell life, as indicated by Prof. Bonafè, also including the coordination of the inflammatory cytokines such as interleukin 6. In fact, this interleukin not only represents one of the main growth factors, but it is also a carrier regulator of the cancer stem cells, for example, those of breast cancer. IL-6 is also a growth factor for cancer cells. These activities are significantly stimulated in the presence of hypoxia.



But what are the intimate mechanisms that regulate the activation of the cancer stem cells in the presence of inflammation?

For more in-depth information click on the following link: www.fondazione-menarini.it/..... and after having logged in, access the multimedia material.

From basic research to clinical trials: a new era for the development of active drugs against cancer at a paediatric age?

Access to drugs for children, and also for adolescents, is still inadequate. Less than one child in ten suffering from a relapse of a non-curable malignant neoplasm, is able to access innovative therapies in Europe. In the 10 years from 2003 to 2013 we have passed from one drug to 13 drugs available for treating malignant neoplasms in paediatric patients. That's only 12 new drugs in 10 years! Consequently, the situation is still inadequate. In order to address these and other problems surrounding the treatment of paediatric patients suffering from malignant neoplasms, Prof. Kearns spoke about the ITCC, the European Consortium for “Innovative Therapies for Children with Cancer”, founded in 2003 and made up of 43 experimental centres and 9 research laboratories located in 11 European Union Member States.

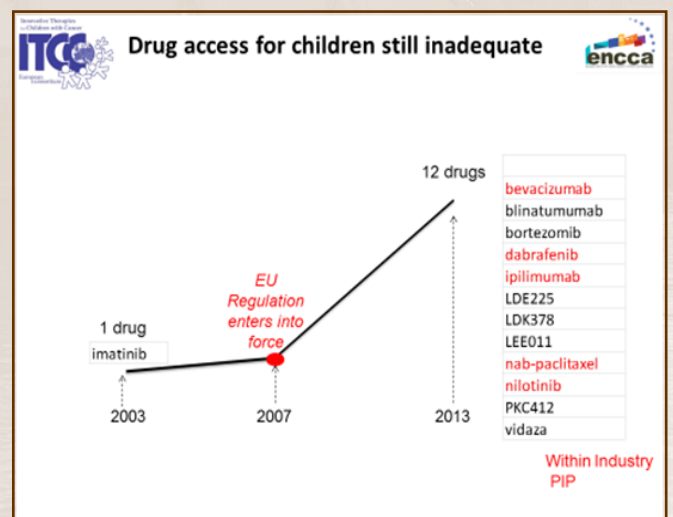


Pamela Kearns
University of
Birmingham (UK)

What strategies are planned by the ITCC over the next five

years from 2015 to 2020, in the aim of improving this situation?

For more in-depth information click on the following link: www.fondazione-menarini.it/..... and after having logged in, access the multimedia material.



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What are the long-term consequences of cancer therapy? What can we do about this situation?

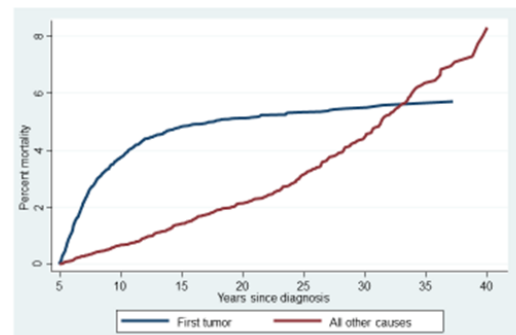
How many people in Europe have survived cancer contracted during childhood? Considering that the prevalence of cancer in childhood is about one in every 1000 subjects and that the population in Europe is approximately 488 million inhabitants, it can be estimated that there are from 400,000 to 500,000 people living in Europe who have survived cancer contracted during childhood, as explained by Prof. Haupt during his talk. If we analyse the mortality rate in this population, it is evident that with the passing of time these subjects

tend to die from causes not directly linked to their cancer per se. It is as though the mortality rate in this population was an indicator of the prevalence of poor health conditions that have been established over time. Could these conditions be the expression of complications linked to the impact of the antineoplastic therapy that have occurred over time and which have a significant impact on everyday life?

What actions can be implemented to intercept these subjects in order to offer them the best possible health assistance over the years?

For more in-depth information click on the following link: www.fondazione-menarini.it/..... and after having logged in, access the multimedia material.

Cause-specific late mortality among
13,920 childhood cancer survivors



OTR, 2014



Riccardo Haupt
Istituto Giannina Gaslini
Genoa (Italy)

These are just some of the topics discussed during the congress works. For further details please visit the website of the Fondazione Internazionale Menarini which contains the full version of all the congress talks.

Visit the link: <http://www.fondazione-menarini.it/Archivio-Eventi/2015/Stem-Cells-Cancer-Immunology-and-Aging/Materiale-Multimediale.....> and after having logged in, access the multimedia material.



Fondazione Internazionale Menarini

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