DIPARTIMENTO DI MEDICINA SPECIALISTICA,
DIAGNOSTICA E SPERIMENTALE

Subject: Research on trisomy 21

Bologna, 1st June 2016

Down Syndrome (DS) is the most frequent human chromosomal disorder, with a frequency of 1 in ~700 births. People with DS have **intellectual disability**, which is present to some degree of severity in all affected individuals and which involves symbolic thought, whereas affectivity and social skills are conserved. It is common for children with DS to arouse a climate of affective intensity greater than the norm.

Although it is a syndrome observed since ancient times, the cause was not known until the '50s of the last century, and instead it was attributed to a "degeneration of the race" as a consequence of supposed "fault" of parents (alcoholism, syphilis). In 1959, the young French doctor Jérôme Lejeune identified the cause of DS as the presence of three copies of human chromosome 21 (Hsa21), instead of the normal two, in the cells of the affected individuals. This condition has been called trisomy 21.

This discovery introduced the notion that a given clinical symptom may be connected to a specific alteration of the human genetic material for the first time, giving origin to the field of **medical genetics**: Prof. Lejeune held the first Chair of Genetics at University of Paris. Moreover, the syndrome is expected to be associated with a spontaneous and unpredictable genetic mutation, with a constant frequency in all populations of the Earth, losing any negative "moral" connotation; the derogatory term "mongolism" was abandoned in favor of "Down Syndrome" or "trisomy 21". Studyng in detail the mechanism of the syndrome becomes possible, in particular how the presence of an extra chromosome 21 can be associated with the symptoms, in view of a possible pharmacological intervention as a therapy for trisomic subjects. Prof. Lejeune firmly believed in the possibility to find a **therapy**, currently investigated by a limited number of research groups.

Our research group aims to systematically study possible **genotype-phenotype relationships in DS** in order to achieve fully understand the genetic mechanisms of the syndrome to therefore identify therapy targets. In the last years, we have identified a new gene not identified in the original report of the complete sequence of chromosome 21, we have performed a large-scale analysis of the structure and expression of chromosome 21, we have designed and developed bioinformatics tools able to process the original information on the structure and expression of genes and genomes. On April 22nd 2016, our paper about the “critical region” for Down syndrome was published in the journal *Human Molecular Genetics*. The study suggests that a “critical region” responsible for the main symptoms of Down syndrome corresponds to only one thousandth of the whole chromosome 21.

The attached research project shows the results of international collaboration obtained by our group and details our ideas for further research on trisomy 21. Funding for this research was influenced, on the one hand, by the limited availability of funds for the local experimental research, and on the other, by the intense efforts toward prenatal diagnosis oriented to selective abortion rather than toward basic and applied research aimed at finding effective therapies. For this reason, every contribution is crucial to support our research activities of the Laboratory.

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Attached documents:
(and accessible through the website http://apollo11.isto.unibo.it/
link at the bottom of the page):

- **Research project:** "21-Maps Projects": A route to the discovery of a cure for trisomy 21 (Down Syndrome). Click on the link "21-Maps_Project.pdf" on the right.

- **Letter of intent for donation (fac simile)** - To make a donation, please send a letter on paper by mail that demonstrates an intention to donate, signed in original and including first and last name (or company name) and address of the sender to our Departement.
In order for the donation to be directed to the Laboratory of Genomics for the research on trisomy 21, this must be specified in the letter of intent, as in the downloadable version by right-clicking on the link "Letter_of_intent.pdf."

At the same time, for donations of "low value" pursuant to art. 783 of the Civil Code, the transfer can be made on the C / C:

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In case of doubts about the interpretation of the "low value" or for any clarification of an administrative nature, you can refer to Dr. Luisa Romagnoli, responsible for administrative management of the Department(e-mail: luisa.romagnoli@unibo.it).

The donation will be followed by a letter of thanks and acceptance by the Director of the Department.

Private individuals, public entities, associations, organizations, foundations and businesses can make donations. It emphasizes the *full deductibility with no income limit or amount of cash donations from the total income of the donor.*

Any specific information about tax deductibility can be found at the link:
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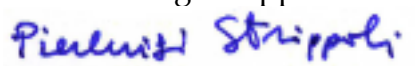
If you wish, you can remain anonymous: in this case, the reference of the donor subject and procedures for delivery will be known only to the Administrative Secretariat. If the name of the donor subject is known, we will be happy to recognize the contribution in the **acknowledgments** at the bottom of the scientific Article that will publish the results obtained thanks to your support, unless the donor wishes that this does not happen (please let us know your will in this regard).

I sincerely thank you very much for your attention, and I am available for any clarification, further information or just to meet, if you wish.

Scientific Supervisor
Prof. Pierluigi Strippoli



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