Two examples of research on Trisomy 21 that show that we might open one day the door to treatments that will save millions of individuals

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Recent advances are showing that it may be possible soon to decipher the underlying genetic and molecular bases for the T21 disability and for creating effective treatments. Different trisomy 21 research groups have already identified candidate genes potentially involved in the formation of specific Down syndrome features.

These advances in turn may help to develop targeted medical treatments for persons with trisomy 21. But not only. From another point of view, Andre Megarbane believes that persons with T21 can guide and help us to found cures for frequent diseases that could affect each one of us.

Alzheimer: Since persons with T21 may develop early-onset Alzheimer disease, we recently investigated the significant CpG sites in patients with T21 from the Jerome Lejeune Institute, and in subjects with Alzheimer disease dementia and controls from the AgeCoDe cohort (German study on Ageing, Cognition, and Dementia). We found that 6 sites were hypermethylated in both T21 and Alzheimer disease patients versus healthy controls, thus reducing the activity of genes present on these sites. One of these loci is located in the *ADAM10* promoter region, a gene that plays a role in reducing the generation of amyloid-β (Aβ) peptides. In confirmation to this, recent studies demonstrate a role for ADAM10 in the ectodomain shedding of low density lipoprotein receptor-related protein 1 (LRP1), a receptor responsible for the transport of Aβ in the brain and thus attenuating Aβ accumulation in the Alzheimer disease brain. We will now follow our T21 cohort and proceed to further studies. If the latter are relevant, we might than confirm the hypermethylation of *ADAM10* as a biomarker for Alzheimer disease in at least patients with T21 and work for the development of new drug targets.

Breast cancer: Studies have shown that persons with T21 are more predisposed to developing hematological tumors than the general population. Yet their risk of developing solid tumors is at least 12 times lower. For instance, breast cancer is almost absent in women with T21, even though this group shows a higher prevalence of known risk factors for breast cancer. In order to identify novel genetic factors implicated in the lower breast cancer frequency observed in women with T21 than in the general population, we compared the transcriptome pattern of women with a homogeneous T21, aged more than 30 years, with or without breast cancer, and tumoral breast cancer tissue of control women with a normal karyotype. Four genes from the same family, namely GIMAP4, GIMAP6, GIMAP7 and GIMAP8, were found to be strongly upregulated in the T21 without breast cancer group compared to the other groups.

Our findings support the hypothesis that GIMAPs may play a tumor-suppressive role against breast cancer in women with T21, opening the possibility that they may also have the same role for other solid tumors. The search for new prognostic factors and hopefully new therapeutic or preventive strategies against breast cancer in women might not be a dream.