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**In search of a functional role for Interstitial Telomeric Sequences**  
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Telomeres are the extremities of linear chromosomes and in vertebrates are composed by tandem repeats of 5'-TTAGGG-3' hexameres. Short stretches of telomeric repeats are also found at the internal sites of the chromosomes where they give rise to the so called Interstitial Telomeric Sequences (ITSs); the data obtained by our group studying ITSs from different species of vertebrates strongly suggest that they arise by telomerase involvement in the repair of DNA double strand breaks that occur during evolution<sup>1,2,3,4</sup>. In order to study whether ITSs can alter gene expression, an extensive search of ITSs in the human genome was carried out. About 40% of the ITSs are contained within introns of genes. The orientation of the telomeric repeats with respect to the sense strand of the gene, the ratio (ITS length)/(intron length), the presence of alternative transcripts, and the presence of predicted or validated regulatory elements was analyzed. Our data show that 63% of the ITSs are in one orientation relative to the coding strand of the gene. About 81% of the ITS-containing introns are involved in alternative splicing, and/or contain an alternative transcription start site (48%) and/or an alternative transcription termination (54%).

These results suggest that the presence of ITS may sometimes influence gene expression and in particular alternative splicing. To test this hypothesis we intend to set up an experimental system to analyze whether the expression or splicing profile of a reporter gene is altered by the presence of an ITS within one of its intron.

The subject of a second line of research regard the involvement of telomerase in DNA double strand break repair, we are going to set up an experimental system to test whether telomerase localizes to laser-induced DNA double strand break sites in order to prove directly its involvement in the DNA double strand break repair process.

#### References

1. Azzalin C, Nergadze SG, Giulotto E, Human intrachromosomal telomeric-like repeats: sequence organization and mechanisms of origin. *Chromosoma* 110 (2001) 75.
2. Nergadze SG, Rocchi M, Azzalin CM, Mondello C, Giulotto E, Insertion of Telomeric repeats at intrachromosomal break sites during primate evolution. *Genome Res* 14 (2004) 1704.
3. Nergadze SG, **Santagostino MA**, Salzano A, Mondello C, Giulotto E, Contribution of telomerase RNA retrotranscription to DNA double-strand break repair during mammalian genome evolution. *Genome Biol* 8 (2007) R260.

4. Nergadze SG, **Santagostino M**, Mondello C, Giulotto E, Insertion of telomerase RNA retrotranscripts at DNA double-strand break sites during mammalian genome evolution. Meeting of the American Association for Cancer Research, San Francisco (California), 6-9 December 2007: B31

#### Full papers

1. Nergadze SG, **Santagostino MA**, Salzano A, Mondello C, Giulotto E, Contribution of telomerase RNA retrotranscription to DNA double-strand break repair during mammalian genome evolution. *Genome Biol* 8 (2007) R260.

#### Abstracts

1. **Santagostino M**, Nergadze SG, Mininni N, Garagna S, Chevret P, Britton-Davidian J, Mondello C, Giulotto E, Involvement of telomerase in DNA double-strand break repair: an evolutionary approach. FISV 2007 8th Annual Meeting, Riva del Garda (Italy), 26-29 September 2007: D07.03
2. Nergadze SG, **Santagostino M**, Mondello C, Giulotto E, Interstitial telomeric repeats in the horse genome molecular markers for population genetics, paternity testing and phylogenetic studies. 7th Havemeyer Horse Genome Workshop, Lake Tahoe, 16-19 August 2007
3. Nergadze SG, **Santagostino M**, Mondello C, Giulotto E, Insertion of telomerase RNA retrotranscripts at DNA double-strand break sites during mammalian genome evolution. Meeting of the American Association for Cancer Research, San Francisco (California), 6-9 December 2007: B31