Identification of CDH1 germline mutations in sporadic gastric cancer patients and subjects at risk to develop gastric cancer

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Germline mutations in the E-cadherin (CDH1) gene are involved in hereditary diffuse gastric cancer (GC). However, the frequency of these variants in sporadic GC and in subjects at risk to develop GC is poorly investigated.

We enrolled 48 consecutive GC pts, 59 first degree relatives (FDR), 20 patients affected by autoimmune atrophic gastritis (AAG) and 52 healthy donors (HD). Screening of the entire coding region and all introns flanking sequences of the CDH1 gene was performed by DNA direct sequencing. Structural modelling studies, bioinformatic tools and immunohistochemistry on new splicing were assessed.

All the missense mutations were found in the extracellular domain of E-cadherin protein: (a) in GC: a novel mutation in exon 6 (p.G274S) with a controversial pathogenic role; 2 already reported in GC families (p.A298T, and p.T470I), and 1 variant in the promoter region (+54 G>C); (B) in FDR: 1 mutation in the promoter region (+71 C>G), 1 in the 5'UTR region (-176 C>T).

1 intronic variant close to exon 5 (IVS4 -18 C>T), a probable new intronic variant, near to exon 1 (IVS1+7 C>T) and 1 intronic variant close to exon 13 (IVS12 -13 T>C) was found in a GC. The last mutation was also found in 1 HD. The variant p.A592T, were detected in all groups.

Our results show that CDH1 mutations with a potential pathological role can also be detected in sporadic GC. This data suggest the need to improve the case study to better investigate contribution of CDH1 variants in sporadic GC and in general population. Moreover, our results highlight that screening for CDH1 mutations could be a tool to define a risk group.

Biography

V. De Re has completed his Ph.D at the age of 25 years from Trieste University and postgraduate studies from Bologna University School of Medicine. She is a manager of experimental and clinical pharmacology, in an IRCCS Institute and coordinator of immunogenetics and proteomics studies. She has published more than 113 papers in reputed journals and serving as reviewer and an editorial board member of repute journal.

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