HOTAIR and gastric cancer: 
a lesson from two meta-analyses

Sharmila FAGONEE 1 *, Marilena DURAZZO 2

1Institute for Biostructures and Bioimages (CNR) c/o Molecular Biotechnology Center, University of Turin, Turin, Italy; 2Department of Medical Sciences, University of Turin, Turin, Italy
*Corresponding author: Sharmila Fagoonee, Institute for Biostructures and Bioimages (CNR) c/o Molecular Biotechnology Center, University of Turin, Turin, Italy. E-mail: sharmila.fagoonee@unito.it

Many factors affect the prognosis of gastric cancer (GC). Invasion and metastasis are, however, the leading causes of death and finding potential genetic involvements becomes crucial. Each result in this context is, hence, of utmost importance for the scientific community. 1

The HOX transcript antisense RNA (HOTAIR) is a human gene located on chromosome 12 and it represents the first example of an RNA expressed on one chromosome that has been found to influence transcription on another chromosome. The HOTAIR gene contains 6232 bp and encodes 2.2 kb long noncoding RNA molecule, which controls gene expression. It is known that high levels of HOTAIR expression in some malignancies, as primary breast tumors, are a significant predictor of subsequent metastasis and death. 2

Recently, the potential role of HOTAIR in gastrointestinal cancers has been investigated in two meta-analyses. 3, 4 The first, published by Miao et al., investigated the correlation between over-expression of HOTAIR and survival of patients with solid tumors. The database search (period June 1st 2007-May 1st 2016) permitted to include 21 studies, with only 2 of these considering patients with GC. 5, 6 Due to this limited sample regarding GC, for their final considerations, the authors analyzed only studies including patients with esophageal squamous cell carcinoma (N.=4) and colorectal cancer (N.=4). 3 The second meta-analysis, published by Liu et al., investigated the association of HOTAIR expression with clinicopathological features and prognosis in patients with GC. 4 The database search (period up to November 15, 2015) permitted to include 10 studies. 5-14 The results showed that high expression of HOTAIR was significantly associated with clinicopathological features, especially depth of tumor invasion, lymph node metastasis, vessel invasion and TNM stage. In addition, aberrant HOTAIR expression was significantly associated with prognosis. 4 Thus, these 2 meta-analyses were, in the first case, incomplete and inconclusive, and in the second case, exhaustive leading to a clear conclusion. Regarding the databases used, these were in part similar (Pubmed, Embase). The difference in other databases (ISI Web of Science, Springer, Chinese National Knowledge Infrastructure and WanFang digital database) employed did not influence the result, except for one study published in Chinese, 10 and included by Liu et al. 4

A meta-analysis is a statistical analysis that combines the results of multiple scientific studies. The basic tenet behind meta-analyses is that there is a common truth behind all conceptually similar scientific studies, but which has been measured with a certain error within individual studies. A key benefit of this approach is the aggregation of information leading to a higher statistical power and more robust point estimate than is possible from the measure derived from any individual study. 15 Thus, the completeness of the sample size is the crucial element when designing a meta-analysis. Unfortunately, there is a trend to perform meta-analyses with heterogeneity on several aspects.
Some examples include the propensity to correlate the expression of some long noncoding RNA molecules either with survival, in patients with cancers of different digestive tracts, or with poor prognosis and lymph node metastasis, in human cancers grouped as arising or not in the digestive system. In conclusion, it is better to avoid meta-analyses with patients suffering from cancers of different organs, considering the fact that different pathogenesis affects these different cancers.

References