European **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences 2018; 22: 5053-5055

Letter to the Editor

Long non-coding RNAs: possible parallel paths by E-cadherin expression in colon cancer development as well as in *Pseudomonas aeruginosa* infection

Dear Editor,

The biological function of long non-coding RNAs (lncRNA) has often been described in the literature in these last years and represents a very interesting field of research in translational medicine[1]. In fact non-coding RNA oligos, > 200 bp, are now thought to have regulatory roles in different fundamental biological pathways and provide cells with an additional layer of response to different environmental stimuli. The regulation of many non-coding RNAs is thought to occur in a variety of human diseases, including cancer progression, bacterial infections and microbial drug resistance. Here we discuss recent research on the molecular functions of long non-coding RNAs in cellular pathways mediating colon cancer, which was described by Gu et al[2] and bacterial infections caused by *P. aeruginosa*[3]. Although the clinical features, etiological aspect and general biological pathways are different for these disease, we suggest that they share a common mechanism in terms of pathological features, namely the interaction between the lncRNA and the E- cadherin pathway during cancer development as well as during bacterial infections[3,4].

Biological Regulation by lncRNAs, a Common Point in cancer and in Bacterial Infections

lncRNAs in eukaryotic cells belong to long intergenic RNAs with transcripts that are not translated into proteins. An interesting aspect is their high abundance within the cell's cytoplasmic area with around more than 30,000 lncRNAs per cell, which suggests that these RNAs play a crucial role in the eukaryotic biological network[1]. These RNA oligos represent a class of non-coding RNAs transcribed by RNA polymerase II (Pol II) and most of these transcripts are adenylated and spliced. As a result, most of them are able to regulate gene expression at the level of transcription or translation, but somewhere lncRNA expression is restricted to precise biological stages or is located in a particular tissue. Traditionally, the study of these lncRNAs falls within cell developmental studies or in the field of tumorigenesis[1], but very recent publications have shown that lncRNAs are also involved in the response against pathogenic bacteria[3]. In the field of human infections, most of the roles of lncRNAs are still unknown, but the scientific results obtained in oncological research could be used to indicate new biological mechanisms in microbial diseases such as *P. aeruginosa* infections i.e. in cystic fibrosis patients.

In this context, the article by Gu et al[2] focalizes on the role of lncRNAs (URHC) in the proliferation and invasion of colorectal cancer cells *in vitro*. The authors proposed that the down-regulation of this molecule in colorectal cancer cells could enhance the expression of a cell junction protein E-cadherin with a subsequent decrease in tumor proliferation and invasion rate. Other authors[4] have reported that an alteration in phosphorylation, as well as the transcription status of E-cadherin, or other junction proteins, are involved in the changes in cell junction associations and in the enhanced paracellular permeability to *P. aeruginosa* infection of the aerial tissues. Our research focused on this crucial role of the intercellular bridge mediated by lncRNA E-cadherin and any subsequent clinical and diagnostic tools in *P. aeruginosa* infections.

P. aeruginosa supports different emerging human/animal infective illnesses and is considered a "superbug". In fact, it is a leading cause of dramatic nosocomial infection, often associated with high drug resistance, especially in surgical, geriatric and oncological hospital

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divisions. In addition, these bacteria cause high morbidity in individuals afflicted with cystic fibrosis. This ubiquitous Gram-negative bacillus has a non-clonal epidemic population structure, but several genotypes (ST111, ST175, ST235, ST244 and ST395) are distributed worldwide and frequently associated with severe outbreaks[5]. These clinical isolates identified as "invasive types" often invade epithelial cells, a process that includes the deactivation of E-cadherin – catenin bridges by phosphorylation with consequent cell-cell junctional gate failure. Figure 1 represents a probable schematic LPS mediated biological pathway described for Gram-negative bacteria[5].

E-cadherins represent a type of cell-cell adhesion molecules belonging to the cadherin group and are involved in the formation of adherent junctions to bind cells with each other (Figure 1). This class -1 of transmembrane proteins is strictly associated in the cytoplasmic domain with catenin proteins. This E-cadherin-catenin complex plays a key role in cellular adhesion and the loss of this function has been associated with greater tumor metastasis, as well as bacterial tissue invasion[4].

Tissue cell junctional gate failure has been shown to be essential in tumorigenesis, especially for tumor and metastasis progression, and a compressive study of this mechanism could be very useful to improve new therapies in cancer research[2]. For example, according to the latest publications, colorectal cancer is the second and third main cause of cancer deaths in women and men. The disease is also characterized by a low survival rate after 5-years and this is why new therapeutic strategies are much needed in this field[6-9].

Usefulness of a Translational Study for lncRNA and E-cadherin

Disruption of the intercellular junctions is a strategy that several microorganisms and neoplastic cells use to their advantage and intervention in these mechanisms by new drugs or new genetic engineering strategies could be useful in several fields of medicine. Although, only a fragmentary study presently exists on the role of lncRNA in severe bacterial infections, such as *P. aeruginosa* in cystic fibrosis, the results obtained in another field by Gu et al[2], promises new light in the research field of microbiology. We speculate a similar mechanism in lncRNA and E-cadherin expression pattern also in the lung-aerial tissues of cystic fibrosis patients, infected with *P.*

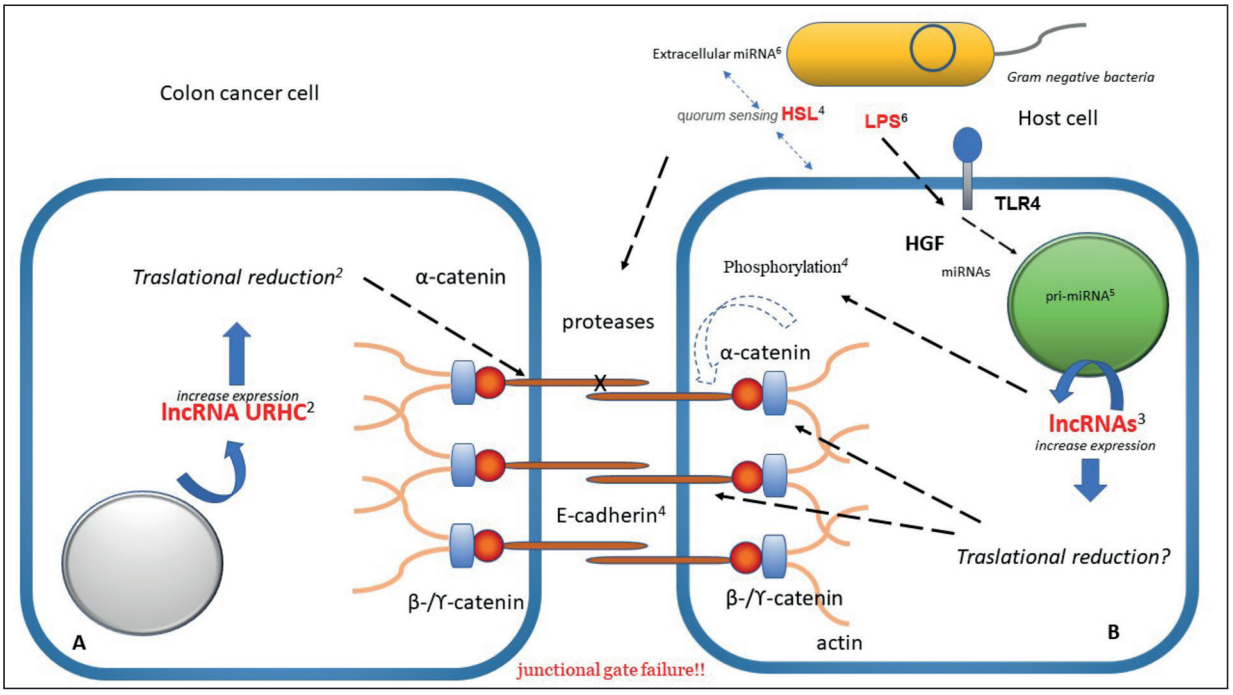

Figure 1. Schematic representation of the role of lncRNA in colon cancer, as described by Gu et al[2], ***(A)*** and a mechanism for P. aeruginosa host infection[3] ***(B)***.

aeruginosa (Figure 1). In this context, lncRNA could be down-regulated by the expression of the E- cadherin pathway in colon cancer[2], as suggested by Gu et al[4], or activate the phosphorylation mechanism in *P. aeruginosa*[4] as described by Vikström et al[4] (Figure 1). As regards its therapeutic application, in both these ways, lncRNA on E-cadherin could be an interesting candidate for the new evolving concept of host-directed therapies to treat bacterial and cancer infections. In particular this cross-talk study could prove interesting for the development of an *in vitro* model cell-bacteria to study new therapeutic tools by using, for example, antisense oligonucleotides (ASOs) against specific lncRNA targets.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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