

Infectious *Leptospira* cross-talk with host catecholamine's during infection

Leptospira belongs to the family Leptospiraceae and the pathogenic species cause a zoonotic disease called leptospirosis. Leptospirosis is a worldwide zoonotic infection of human and veterinary concern, with approximately over one million cases reported annually. This disease has a higher occurrence in the tropical and subtropical regions. Humans are infected with the bacteria through direct or indirect contact with contaminated environments and exhibit a wide range of clinical manifestations, ranging from a mild influenza-like illness to a severe Weil's disease. The sever form of leptospirosis affects multiple vital organs like liver, kidney, and lungs. In wild or domestic animals, leptospirosis my results into reproductive complications like abortion, stillbirth, and a decrease in the growth rate as well as in milk production resulting in huge economic losses. Leptospirosis is severely underdiagnosed owing to its symptoms being similar to other diseases. There is also a very limited availability of reliable and rapid diagnostic tests which makes it very difficult to confirm the disease.

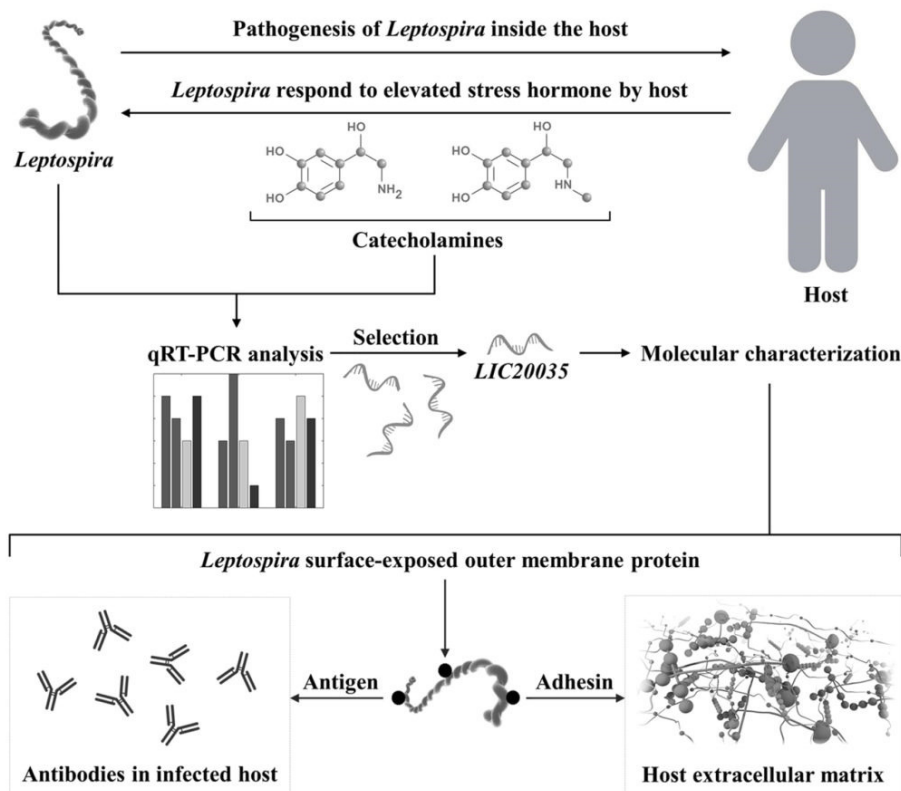


Fig. 1. The characterization of LIC20035 of *L. interrogans* modulated by the host catecholamine. One of the genes differentially transcribed in the presence of catecholamines was characterized as an adhesion and a serodiagnostic candidate marker for leptospirosis. LIC20035 was determined to be a surface-exposed outer membrane protein with a binding affinity to a vast range of host extracellular matrix components. The recombinant LIC20035 could also be serologically detected using leptospirosis infected serum samples.

Microbial endocrinology studies demonstrate that many pathogenic bacteria can respond to the neuroendocrine environment of the host and upon infection, hijack the host neuro-hormonal products of physiological stress response such as catecholamines in humans and animals. Catecholamines (Epinephrine [Epi] and norepinephrine [NE]) are identified as the neuroendocrine mediators of fight and flight response of the host. Pathogenic bacteria intercept the host catecholamines and use them as an environmental cue to alter its growth and virulence during infection. The present study aimed at understanding the differential transcription of genes encoding membrane proteins of *Leptospira interrogans* on exposure to host-stress hormone catecholamines, under *in vitro* condition. The transcript analyses in response to Epi/NE and its antagonist propranolol (PO) using the real-time reverse transcription-PCR (qRT-PCR) technique of genes encoding membrane proteins of *L. interrogans* was investigated. It is anticipated that this approach will facilitate the identification of membrane proteins responding to host chemical signals with the potential to serve as new serodiagnostic antigens, and probable adhesins. As an initial step towards the comprehensive understanding of the effect of catecholamines on the transcription of membrane proteins of *L. interrogans*, one of the seven genes viz. *LIC20035/LB047* showing a response to catecholamines was further characterized.

There was no impact of catecholamine supplementation on the *in vitro* growth pattern of *L. interrogans*, however, 7 genes out of 41 selected, were differentially transcribed in the presence of catecholamines and the effect of which was restored to the basal level in the presence of its antagonist propranolol. The comprehensive analysis of one of the differentially down-regulated protein *LIC20035/LB047* due to catecholamine supplementation showed immunogenic and adhesin property to host extracellular matrices. Protease-accessibility assay and phase-partitioning of *L. interrogans* proteome describe *LIC20035/LB047* to be an outer membrane surface-exposed protein. The recombinant-*LIC20035* protein can be serologically detected using human and bovine sera tested positive for leptospirosis. Moreover, the recombinant-*LIC20035* can bind to diverse host extracellular matrices with a higher affinity towards collagen and chondroitin sulfate. These results show that one of the host factors catecholamines is being adapted by *Leptospira* to disseminate in various host tissues. Future work on host-pathogen chemical signaling is needed for the development of wide-range of disease control approaches. We have identified a novel outer membrane protein of *L. interrogans* serovar Copenhageni strain Fiocruz L1-130, *LIC20035* which can serve as an adhesin during host tissue dissemination and can also be utilized as a sero-diagnostic marker for leptospirosis across a wide range of hosts.

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[Catecholamine-Modulated Novel Surface-Exposed Adhesin *LIC20035* of *Leptospira* spp. Binds Host Extracellular Matrix Components and Is Recognized by the Host during Infection.](#)

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