Editorial

The luminal-basal paradigm in the urothelial cancer: hope for individualized approach

Leonardo Oliveira Reis

Urologic Oncology Division, Pontifical Catholic University of Campinas, PUC-Campinas, Campinas-SP, Brazil

Correspondence to: Prof. Dr. Leonardo Oliveira Reis. Pontifical Catholic University of Campinas, PUC-Campinas, Av. John Boyd Dunlop, s/n CEP 13060-904, Campinas-SP, Brazil. Email: reisleo.l@gmail.com.

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While restricted to less than 10% of the urothelial cell carcinoma spectrum, bladder micropapillary carcinoma (MPUC) is associated with shorter survival due to early and wide metastatic chemo resistant spread. Such ominous behavior makes it an interesting model to identify new diagnostic, prognostic, and therapeutic targets based on unique gene expressions and molecular features associated with the aggressive nature of the disease (1).

An in-depth genetic analysis of potential mechanisms implicated in MPUC cellular transformation suggests that it develops almost exclusively from luminal conventional urothelial carcinoma, characterizing by down regulation of miR-296 and activation of the oncogene chromatin remodeling complex RUVBL1. Most (98%) MPUC are of the luminal type, being the wild-type p53-like the most aggressive variant of the disease. Additionally, luminal subtype and micropapillary expression signature was present in the conventional component of the tumors that contained foci of MPUC and a small subset of conventional bladder cancers expressing a micropapillary signature (3.9%) were all of the luminal type (2).

As a continuum to the above-mentioned contributions in the muscle invasive bladder cancer (MIBC) scenario where conventional urothelial carcinoma can be subdivided (almost in half) into two major groups: luminal (of which 1/3 as p53-like) and basal subtypes (2), similar classification also substantiates such premises in the field of non-muscle invasive bladder cancer (NMIBC) heterogeneity as luminal-like (class 1 and class 2) and basal-like (class 3). Patients with stage progression tend to present a basal to luminal shift and aggressive disease was mostly classified as luminal, either at an early stage or during disease progression; however, if the three classes represent transitions or three independent developmental pathways cannot be assured so far (3).

Obviously, functional experiments and larger cohorts are necessary before the cause and effect relations are confirmed for such a wide experimental strategy. If confirmed, randomized trials will validate the clinical impact of subclass assignment and will positively encourage advances in the understanding of oncoimmunology related to such spectrum in this immunogenic disease.

The vital piece is that the paradigm of luminal (p53-like subtype or not) and basal subtypes, originally identified in human breast cancers, may represent attractive strategy to an individualized surveillance and therapeutic approaches in urothelial cancer upfront (4,5).

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Footnote

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