Multi-level analyses reveal complexity of physiological alterations accompanying bivalve transmissible neoplasia (BTN) in *Macoma balthica* clams

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Bivalves transmissible neoplasia (BTN) is a form of disseminated neoplasia of haemocytic origin. It is distinguished by the ability of neoplastic cells (NCs) to migrate between individuals of a single species by horizontal transfer and develop tumorigenesis in healthy individuals, increasing premature mortality. It affects marine organisms of great ecological and economic importance. *Macoma balthica* is a clam species inhabiting the Gulf of Gdańsk (southern Baltic Sea), largely affected by BTN, as up to 90% prevalence of the disease has been observed in some areas of the gulf. Therefore, this species provides a perfect disease study model. Available data on bivalves prone to BTN suggests that it is characterized by multilevel dysfunctions, yet complete knowledge on pathophysiology as well as etiology of the disease remains scarce. Here, we present results of multi-technical approach to define neoplasia based on 10 healthy and 10 BTN-positive *M. balthica* individuals on cytological, histological, functional as well as molecular levels. Cytological analyses revealed morphological alterations typical for neoplastic cells (hypertrophy, anaplasia and large nucleus volume). In addition, high level of infiltration of NCs within soft tissues was observed during histology studies. Flow cytometry analyses of NCs showed alterations within immune components, including impaired phagocytic activity and increased level of reactive oxygen species. Preliminary results revealed that transcriptomic profile of NCs was characterized by altered expression among genes responsible for essential cellular processes such as DNA repair and apoptosis. These findings constitute an important part of defining the pathophysiological characteristics of transmissible neoplasia in bivalves.