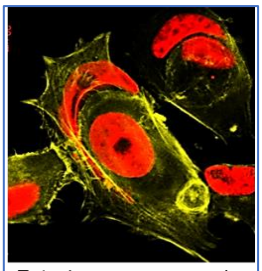
Cancer affects around 180,000 people a year in Poland alone. Its diagnosis and treatment are a significant social and clinical problem, due to the limited number of fully effective therapeutic strategies, resulting, among others, from the still poorly understood biology of cancer cells.



Entosis, process by which one cell is engulfed by another cell. *(Fot. A. Gaweł)*

It is considered that one of the processes by which cancer cells survive the host immune response and chemotherapies is their ability to form "entosis" (cell-in-cell structures), the main features of which are presence of one cell inside another and a crescent-shaped nucleus surrounding the inner cell (pictured right).

Entotic cells are observed in various tumor tissues, and their number is associated with tumor stage and progression. In our published studies using clinical specimens, we confirmed high incidence of entoses in primary and metastatic breast cancer tissue and showed that the total number of entoses in metastatic tumors is significantly enhanced. This suggests that an increase in the number of entotic structures within cancerous tissue may be associated with worse prognosis. Therefore, changes in the frequency of formation of entotic structures may be considered as a new biomarker informing about the development/stage of disease progression. However, the molecular mechanisms leading to the formation of entotic structures are still not well-defined. In particular, there is little knowledge of the proteins and major signaling pathways regulating the process of cell internalization.

Therefore, our goal is to define new significantly deregulated genes in entotic cells. We assume that: (i) the gene expression profile of entotic cells is different from that of non-entotic cells, (ii) and genes whose expression is altered in entotic cells may play a key role in formation of "cell-in-cell" structures.

The study will use a panel of advanced molecular biology tools. The use of a flow cytometer will allow us to select entotic structures formed by the stained cancer cells. Further analysis using the next-generation sequencing technique will enable us to determine the gene expression profile of the entotic cells. The data will be verified using cell staining and confocal microscopy, as well as silencing the expression of selected genes, and PCR and Western blot techniques.

Elucidation of the new genes and signaling pathways affecting the formation of entotic figures will result in discovery of the molecular factors responsible for formation of entotic structures. We believe that some of the identified drivers of entosis may be clinically beneficial as specific biomarkers indicating the biological status/advancement of the tumor.