

## REDOX-METABOLIC SIGNATURE OF BREAST CANCER

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Redox and metabolic homeostasis are essential for maintaining the body's energy needs. They represent an integrative, evolutionarily conserved response, whose molecular mechanisms have been constantly evolving and adapting to the altered microenvironment, especially in aerobic organisms. This refers to the maintenance of homeostasis in both physiological and pathological conditions, from metabolic disorders, diabetes, obesity, cardiovascular and neurodegenerative diseases, to cancer. Precisely in cancer, redox-metabolic reprogramming is a key hallmark of neoplastic transformation that allows it to create an adaptive environment. This is strongly coupled to the interaction of cancer cells with their microenvironment. In breast cancer, the principal component of the tumor milieu is adipose tissue. Adipocytes and cancer cells are in cooperation rather than in competition. Establishing or disrupting their relationship is crucial for the initiation and progression of breast cancer, as well as for metastatic potential and therapeutic resistance. However, several issues regarding the production of reactive oxygen species, the organization of antioxidant defense, and metabolic reprogramming in breast cancer are unresolved. This is especially true of the role of redox-metabolic transcription factors involved in cancer and adipose tissue reprogramming, primarily Nrf2 (nuclear factor erythroid 2-related factor 2). This is an attempt to review and provide an overview of the current state and perspectives in discovering the mechanisms of redox-metabolic reprogramming in breast cancer.

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## REDOKS-METABOLIČKI POTPIS KANCERA DOJKE

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Redoks i metabolička homeostaza su esencijalni za održanje energetske potrebe organizma. Predstavljaju integrativni, evolutivno konzerviran odgovor, čiji su se molekularni mehanizmi neprekidno razvijali i adaptirali na izmenjenu mikrosredinu, posebno kod aerobnih organizama. To se odnosi na održanje homeostaze kako u fiziološkim, tako i patološkim stanjima, od metaboličkih poremećaja, dijabetesa, gojaznosti, kardiovaskularnih i neurodegenerativnih bolesti, do kancera. Upravo u kanceru redoks-metaboličko reprogramiranje predstavlja ključno obeležje neoplastične transformacije koje mu omogućava da kreira adaptivno okruženje. To je snažno spregnuto interakcijom kancerskih ćelija sa mikrosredinom. Kod kancera dojke osnovna komponenta tumorskog miljea je masno tkivo. Adipociti i kancerske ćelije su pre u kooperaciji nego kompeticiji. Uspostavljanje ili narušavanje njihovog odnosa je ključno za inicijaciju i progresiju kancera dojke, kao i za metastatski potencijal i terapijsku rezistenciju. Međutim, pitanja u vezi produkcije reaktivnih vrsti kiseonika, organizacije antioksidativne odbrane i metaboličkog reprogramiranja u kanceru dojke su ostala otvorena. To se posebno odnosi na ulogu redoks-metaboličkih transkripcionih faktora uključenih u reprogramiranje masnog i kancerskog tkiva, u prvom redu Nrf2 (*eng.* nuclear factor erythroid 2-related factor 2). Ovo je pokušaj da se sagleda i pruži pregled sadašnjeg stanja i perspektiva u otkrivanju mehanizama redoks-metaboličkog reprogramiranja u kanceru dojke.

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