A systems biology approach to predict amino acid homeostasis in cancer cells

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Many cancer cells depend on glutamine as they use the glutaminolysis pathway to generate building blocks and energy for anabolic purposes. As a result, glutamine transporters are essential for cancer growth and are potential targets for cancer chemotherapy, with ASCT2 (SLC1A5) being investigated most intensively. Many cancer cells express a set of glutamine transporters including SNAT1 (SLC38A1), SNAT2 (SLC38A2), SNAT4 (SLC38A4), LAT1 (SLC7A5), and ASCT2 (SLC1A5). Using 143B osteosarcoma cells as an example, we could demonstrate that net glutamine uptake did not depend on ASCT2, but required expression of SNAT1 and SNAT2. Deletion of ASCT2, did not reduce cell growth but caused an amino acid starvation response and up-regulation of SNAT1 to replace ASCT2 functionally. Using these data we could develop a mathematical algorithm that predicts intracellular amino acid concentration based on transport activities and metabolism of selected amino acids.