P-glycoprotein

P-glycoprotein 1 (permeability glycoprotein, abbreviated as P-gp or Pgp) also known as multidrug resistance protein 1 (MDR1) or ATP-binding cassette sub-family B member 1 (ABCB1) or cluster of differentiation 243 (CD243) is an important protein of the cell membrane that pumps many foreign substances out of cells. More formally, it is an ATP-dependent efflux pump with broad substrate specificity. It exists in animals, fungi, and bacteria and likely evolved as a defense mechanism against harmful substances.

The goal of Brukner et al. was to measure the absolute differential abundance of key drug transporters in human epileptogenic brain tissue and to compare them between patients and at various distances from the epileptogenic zone within the same patient. Transporter protein abundance was quantified in brain tissue homogenates from patients who underwent epilepsy surgery, using targeted proteomics, and correlations with clinical and tissue characteristics were assessed. Fourteen brain samples (including four epileptogenic hippocampal samples) were collected from nine patients. Among the quantifiable drug transporters, the abundance (median, range) ranked: breast cancer resistance protein (ABCG2/BCRP; 0.55, 0.01-3.26 pmol/g tissue) > P-glycoprotein (ABCB1/MDR1; 0.30, 0.02-1.15 pmol/g tissue) > equilibrative nucleoside transporter 1 (SLC29A1/ENT1; 0.06, 0.001-0.35 pmol/g tissue). The ABCB1/ABCG2 ratio (mean 0.27, range 0.08-0.47) was comparable with literature values from nonepileptogenic brain tissue (mean 0.5-0.8). Transporter abundance was lower in the hippocampi than in the less epileptogenic neocortex of the same patients. ABCG2/BCRP and ABCB1/MDR1 expression strongly correlated with that of glucose transporter 1 (SLC2A1/GLUT1) (r = 0.97, p < 0.001; r = 0.90, p < 0.01, respectively). Low transporter abundance was found in patients with overt vascular pathology, whereas the highest abundance was seen in a sample with normally appearing blood vessels. In conclusion, drug transporter abundance highly varies across patients and between epileptogenic and less epileptogenic brain tissue of the same patient. The strong correlation in the abundance of ABCB1/MDR1, ABCG2/BCRP, and SLC2A1/GLUT1 suggests variation in the content of the functional vasculature within the tissue samples. The epileptogenic tissue can be depleted of key drug transport mechanisms, warranting consideration when selecting treatments for patients with drug-resistant epilepsy 1 .

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Brukner AM, Billington S, Benifla M, Nguyen TB, Han H, Bennett O, Gilboa T, Blatch D, Fellig Y, Volkov O, Unadkat JD, Ekstein D, Eyal S. Abundance of P-glycoprotein and Breast Cancer Resistance Protein Measured by Targeted Proteomics in Human Epileptogenic Brain Tissue. Mol Pharm. 2021 May 19. doi: 10.1021/acs.molpharmaceut.1c00083. Epub ahead of print. PMID: 34008992.

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