Numerous chemical compounds of natural origin have biological activity. For a long time, they were the only drugs available to humans and they still constitute an inexhaustible source of inspiration for modern pharmacology. They are a structurally privileged group of drugs, because they have high affinity to structures occurring in living organisms. My scientific interests focus on the anticancer activity of natural compounds, and I'm mostly interested in compounds that can be used in the treatment of melanoma.

Infusion of **feverfew** leaves (łac. *Tanacetum parthenium*) has been used in natural medicine for centuries as an antipyretic, analgesic and anti-migraine agent. Clinical studies have shown that the main ingredient determining its biological activity is the sesquiterpene lactone, parthenolide. It also has anticancer activity in many types of cancer, which has been proven in numerous *in vitro* and *in vivo* preclinical studies. A very important feature of parthenolide is that it does not affect normal cells, unlike most drugs used in oncological therapy. Parthenolide acts mainly by inhibiting the activity of the transcription factor NF-κB, which is constitutively active in many types of cancer. It has been proven that parthenolide also affects the activity of proteins associated with the formation and development of cancer, including proteins from the STAT, MAPK and JNK families and p53 protein, induces DNA hypomethylation and the accumulation of reactive oxygen species.

Parthenolide caught my attention because of its wide and varied biological activity, which makes it an excellent complement to standard oncological therapies. To date, it has been proven that parthenolide has a synergistic effect with drugs used in intestinal, breast, lung, pancreatic and liver cancer, as well as in many types of leukemia. Moreover, it sensitizes cancer cells to chemotherapy and radiotherapy by inhibiting the activity of NF-κB, and overcomes drug resistance, both intrinsic and acquired (*Sztiller-Sikorska, Czyż, 2020, Pharmaceuticals*). Our team has shown that parthenolide is also active in melanoma, which is a high treatment-resistant cancer (*Czyż i wsp., 2010, Br J Pharmacol*). We observed that parthenolide acts synergistically with dacarbazine, a drug used in the treatment of melanoma (*Koprowska i wsp., 2013, Anticancer Drugs*) and increases the effectiveness of doxorubicin (*Woźniak i wsp., 2013, Anticancer Res*).

The presence of heterogeneous, phenotypically and genotypically, cell subpopulations within the tumor might be one of the reasons for failure in melanoma treatment. Commercially available cell lines, in which all cells represent the same phenotype, do not reflect tumor heterogeneity. In our Department, we have the unique opportunity to conduct research on heterogeneous populations of melanoma cells derived from tumors removed during surgical interventions and characterized by our team (*Sztiller-Sikorska i wsp., 2012, Melanoma Res; Sztiller-Sikorska i wsp., 2015, Lab Invest; Hartman i wsp., 2018, Mol Carcinog*). Using these cells we have demonstrated e.g. that parthenolide effectively removed cells with stem cell characteristics from the melanoma population (*Czyż i wsp., 2013, Cancer Biol Ther*).

The great therapeutic potential of parthenolide encouraged us to look for other naturally occurring compounds that have anticancer activity in melanoma. Screening of 120 compounds from the US National Cancer Institute library containing compounds of natural origin (The Natural Products Set II) allowed the selection of many active substances, including several that, like parthenolide, caused the elimination of the pool of cells with stem cell characteristics.