Book Reviews

Elena Moncevičiūtė-Eringienė.
Cancer as an Evolutionary Cell Variety Resistant to Chronic Damage.
Vilnius: Lietuvos mokslas 2000, 268 p. (in Lithuanian)

In the monograph the author proposes a new conception of the mechanisms of general evolutional persistent resistance of cells to chronic damaging factors as being closely related with the development of tumourous cells. The evolutional malignant resistance has an immense power to drive and control the process of carcinogenesis and success of microbial and tumour chemotherapy. So, the mechanisms of multixenobiotic resistance (MXR) and multidrug resistance (MDR) have common features in the formation of acquired resistance in microorganisms, carcinogenesis, tumour metastases and chemotherapy or irradiation. ATP-dependent membrane P-glycoprotein and multidrug rezistance-related protein as MDR efflux pumps, glutathione S-transferases and other products of evolutionary resistance-related genes arose for exportation and detoxication of cytotoxic xenobiotics and drugs. On the one hand, this evolutionary MXR as a common biological defence mechanism is a first "driving" power to conserve homeostasis of cells, tissues and organs. On the other hand, mutation, selection and simplification of properties are the second mechanism of genetic, functional and morphological changes in tumour cells which regress to a more primitive mode of existence (atavism) for adaptation and survival.

First, this phenomenon of malignant resistance is characteristic of microbial cells whose resistance to antibiotics and other chemotherapeutic drugs appears through transmembrane transporters. The structure and function of some multidrug transporters of resistance are conserved from microorganisms to mammalia.

As somatic cells are exposed to carcinogens and develop into tumour cells, they also acquire resistance to the toxic effects of carcinogens through these same transmembrane transporters. The cancerous cells have acquired persistant evolutionary resistance to chemotherapy drugs or irradiation by the same ABC-type drug transporters encountered in prokaryotic and eukaryotic cells.

All resistant cells have the following characteristics: simplified metabolism, genetic, biochemical and morphological properties, lower requirements to their nutrient medium, accelerated growth, parasitic qualities, invasiveness, weakening intercellularties. It is as if they regress into a more primitive mode of existense (into atavistic reaction of adaptation) to survive under unfavourable conditions. The phenomenon of accelerated growth is an expression of the response of resistant cells to the injuring factors. Somatic cells resistant to carcinogens and the cells which undergo progression to more malignant types under the influence of drugs become in some properties similar to unicellular organisms or to forms of the latter which are resistant to damaging factors. The more primitive the cells become, the better they survive. The multidrug resistance-related genes have a complex role in the formation of resistance in microorganisms, carcinogenesis, tumour progression and chemotherapy. Thus, cancer is a special case of the evolutional resistance of cells to damaging factors.

The basis of author's conception is supported by:

1) similarity of mammalian P-glycoprotein to bacterial cytoplasmic proteins (HlyB or NdrA) which have the ability to remove some substances from somatic cells and microbes;

2) conservation of lactococcal protein, LmrA, as a multidrug resistance efflux pump, from bacteria to man;

3) structural similarity and functional interchangeability of lactococcal protein, LmrA, and human P-glycoprotein;

4) presence of active multidrug resistance gene products of P-glycoprotein type in one of the multiple mechanisms of fungi resistant to azole antifungals;

5) homologs of human P-glycoprotein (P-gp) and multidrug resistance-related protein (MRP) found in microorganisms such as *Lactococcus lactis, Candida albicans, Plasmodium falciparum, Saccharomyces cerevisiae*;

6) the hereditary multixenobiotic resistance (MXR) mechanism in aquatic organisms from pristine areas;

7) similarity of the multixenobiotic resistance (MXR) of marine and freshwater organisms (worm, sponge, mussel, clam, oyster, snail, fish) to P-glycoprotein of mammalia;

8) mechanism of multixenobiotic resistance (MXR) in aquatic invertebrate cells identical to multidrug resistance (MDR) in tumour cells;

9) expression of P-glycoprotein constitutively in normal tissues at a low level;

10) similarity of P-glycoprotein expression in normal and tumourous cells;

11) identical antigenic properties of P-glycoprotein in all mammalia;

12) overexpression of P-glycoprotein in mammalian cells associated with reduced drug accumulation in cells;

13) link of glutathione S-transferases to the detoxification of environmental chemicals and carcinogens;

14) overexpression of the level of glutathione S-transferases in normal and tumourous cells after exposure to cytotoxic drugs;

15) link of overexpression of glutathione S-transferase enzymes to the increased resistance caused by cytotoxic chemicals;

16) dependence of resistance to chemotherapy of experimental tumours on their ability of accelerated growth;

17) direct link between aquired drug resistance and metastases;

18) resistance and rapid regrowth of malignant cells between the cycles of chemotherapy;

19) simplication of genetic, morphological and functional properties and metabolism in both resistant bacterial and tumorous cells;

20) the evident complex role of MDR-related genes in chemotherapy, carcinogenesis and tumour progression.

Elena Moncevičiūtė-Eringienė

VĖŽYS – LĖTINIAM ŽALOJIMUI ATSPARIŲ LĄSTELIŲ EVOLIUCINĖ ATMAINA (MONOGRAFIJOS APŽVALGA)

S a n t r a u k a

Monografijoje pateikiama nauja navikinių ląstelių formavimosi koncepcija. Jos esmė grindžiama bendrabiologinio evoliucinio rezistentiškumo žalojantiems veiksniams mechanizmais, kurie bakterijose atsirado laipsniškai prieš 4,5 milijardo metų ir evoliucijos raidoje buvo perduoti pirmuonių, bestuburių, žinduolių ląstelėms. Jie, įvairiose evoliucijos pakopose padėję gyvybei išlikti nepalankiomis sąlygomis, pažeistose ląstelėse esant homeostazės sutrikimams tampa varomąja kancerogenezės proceso jėga. Tad piktybėjančiose ląstelėse vykstantys genetiniai, morfologiniai ir funkciniai pokyčiai yra antriniai, atspindintys besiformuojančius paprastėjimo procesus. Kad išgyventų, ląstelės tarsi grįžta evoliucijos laiptais atgal į atavistinės raidos būklę.Tokios primityvios ląstelės nebeklauso organizmo reguliuojančių mechanizmų ir įgyja polinkį greičiau augti. Dėl to akivaizdžiai formuojasi bendrasis piktybiškas atsparumas daugeliui negimininių tiek struktūros, tiek funkcijos atžvilgiu kancerogeninių veiksnių. Todėl svarbu ne šalinti įgytą rezistentiškumą visuose lygiuose, o profilaktinėmis priemonėmis užkirsti kelią jo formavimuisi, saugant visų evoliucijos pakopų organizmus ir jų ląsteles nuo žalojimo ir intensyviai šviečiant žmones apie rezistentiškumo žalojantiems veiksniams pasekmes – vėžinio proceso formavimąsi ir navikinių ligų gausėjimą.

Knyga skiriama onkologijos mokslo tyrinėtojams, gydytojams onkologams, patofiziologams, imunologams, biologams, visų sričių praktikos gydytojams ir medicinos bei biologijos studentams.