Repurposing Another Drug: Metformin Could Be Useful for Some Breast Cancer Treatments

By Ruth Kava — December 18, 2017

Antibiotic-resistant bacteria is a well-known phenomenon, which has been plaguing us since right after penicillin was invented. But resistance is not limited to microbes. Human cells can also become resistant to the drugs used to treat them. Such is the case with some types of breast cancer cells. Writing in *PLOS One*, Dr. Gerald Davies from the University of Saskatchewan, in Canada, and colleagues report finding that metformin, a drug used to treat type 2 diabetes, has some efficacy in treating drug-resistant breast cancer cells *in vitro* and in mice.

The authors note that cancer cells may be resistant to a drug or drugs (multiple drug resistant, or MDR) at the beginning of drug treatment or may become resistant during the course of treatment. And resistance to one drug, they state, often is an indication that there will be resistance to several. This necessitates additional types of drug therapy, which are likely to be less effective or tolerable than the original. Thus understanding the genesis of such resistance or how to treat it is of great importance.

The investigators explain "Well-recognized molecular mechanisms of resistance are known and have been recently reviewed. At the forefront is the ABC family of drug-efflux pumps whose over-activity has been consistently associated with drug resistance." These cellular pumps (1) thus remove drugs from cells before they can affect the cells' metabolism. They also note that pharmaceutical inhibitors of the pumps have high toxicities and don't account for all the possible resistance mechanisms.

In one set of experiments, Dr. Davies and colleagues tested breast cancer cells that were and were not resistant to a commonly used chemotherapeutic drug, doxorubicin (DOX). They found a
dose-responsive effect of metformin on depressing the proliferation of the cancer cells on both the non-resistant and DOX-resistant cells — the effect was significantly greater in the non-resistant cells, as would be expected. Following up on these results, they treated parental and DOX-resistant cells with metformin and/or DOX: as expected, the resistant cells’ proliferation rate was not affected by DOX treatment, while the cells from the parental line slowed. Again, metformin alone decreased proliferation in both types of cells, but more so in the parental line cells. When DOX was added to the metformin, there was the greatest diminution of proliferation in the parental line cells, and there again was a response in the DOX-resistant cells too.

In subsequent mouse studies, the investigators injected mice with DOX-resistant tumor cells and then treated them with metformin. Control mice received injections of the metformin vehicle only. After 72 hours, the tumors were harvested and evaluated. They found that the metformin significantly reduced the expression of cancer-related proteins significantly compared to control mice.

Thus, these researchers presented data supporting the novel use of metformin as an anti-proliferation treatment for some types of breast cancers, even if those malignancies were resistant to at least one commonly used chemotherapeutic agent. More research is needed before this treatment modality is ready for ‘prime time’ use in humans, of course, however, these results make us wonder what other drugs are potentially useful in the fight against breast cancer and other forms of cancer.

NOTE:

(1) Efflux pumps are well known in microbiology. They are one of the methods by which bacteria develop resistance to antibiotics, especially those in the tetracycline class.