MedicalXpress

# Using miRNA to cure mature B cell neoplasia

August 9 2017

Credit: Prof. Almudena Ramiro

Almost half of patients with mature B cell neoplasia are faced with the ineffectiveness of existing treatments. However, they may soon benefit from new therapeutic tools relying on miRNA—a small non-coding RNA molecule involved in RNA silencing and post-transcriptional regulation of gene expression.

This strategy could save about 26 000 patients every year. Instead of multidrug R-CHOP chemotherapy for patients with mature B cell neoplasia such as diffuse large B Cell Lymphoma, Burkitt Lymphoma and B cell Chronic Lymphocytic Leukaemia, the EU-funded HEAL-BY-MIRNA (microRNA replacement therapy for mature B cell neoplasias) project offers an innovative approach using an miRNA specific to mature B cells whose expression is lost in mature B cell neoplasia patients.

By re-introducing this miRNA in lymphoma cells, the ateam led by Prof. Almudena Ramiro is hopeful that they will soon be able to treat patients resistant to R-CHOP or victims of relapses.

## What would you say are the main strengths and weaknesses of current treatments for B cell neoplasia?

B cell neoplasia is currently treated mainly by radiation and R-CHOP multidrug chemotherapy. This multidrug therapy can be very effective, but it has a number of significant limitations, including the fact that a fraction of cases show resistance to the treatment. For instance, in the case of 'Diffuse large B cells lymphoma' (DLBCL), the most prevalent of aggressive lymphomas, around 40-45 % of patients do not respond to R-CHOP. Another major problem is that a proportion of B cell neoplasia patients relapse after an initial response to R-CHOP treatment. Furthermore, this treatment is highly intensive and has a high level of associated toxicity.

## How do you explain the fact that chemotherapy is often ineffective?

The two main reasons thought to be responsible for chemotherapy ineffectiveness in cancer treatment are the non-specificity of the cytotoxic action of chemotherapy, which also affects healthy tissue, and the capacity of the tumour to generate mutational variants resistant to the chemotherapy treatments.

## Why focus the search for alternative therapies on miRNAs specifically?

miRNAs are targeted, biologically active molecules that have certain characteristics that make them very attractive candidates as anti-tumoural therapeutic tools: their small size and stability, the fact that they can easily be chemically modified, and the fact that they are less susceptible to drug-resistance development because they modulate gene expression networks rather than individual genes. They are also less likely to show toxic effects, as miRNAs target clusters of genes based on a specific nucleotide sequence.

## What can you tell us about the project's results so far?

Unfortunately we cannot comment on specific results here because they are currently in the process of being protected by a patent, but I can say that we are really excited about the results obtained so far and we believe that they can lead to the development of a novel and more effective therapeutic protocol for the treatment of B cell neoplasia in the future.

## Did the effectiveness of the proposed approach meet your initial expectations?

Yes, we think the approaches of the proposal are adequate for performing preclinical assays to test the effectiveness of miR-28 analogues for lymphoma treatment.

## When could this proposal lead to a new treatment option for patients?

The development of new clinical drugs is a very well established and regulated process that consists of three different stages. We believe that the promising results we have obtained with miR-28 synthetic analogues

in blocking lymphoma growth in preclinical in vivo models justify the initiation of a phase I clinical trial.

In this sense, we are perusing the interest of biotech companies in the development of a new product based on synthetic miR-28 analogues to start this first phase. Phase I clinical trials usually involve the engagement of 20 to 100 volunteers. Depending on the results obtained in this initial trial, the product would be assessed in subsequent phase II and III clinical trials, which involve larger numbers of individuals and a period of time that ranges from two to six years.

## Are you already planning for any follow-up research?

Absolutely, we are planning on assessing different aspects of an miR-28 analogue therapy for lymphoma treatment in preclinical in vivo models of lymphoma: its efficacy on chemotherapy-resistant lymphomas, its effectiveness in different protocols of sequential or combined administration with chemotherapy and the characterisation of the molecular processes that lead to the generation of treatment-resistant lymphoma cells.

**More information:** Project page: cordis.europa.eu/project/rcn/203333

Provided by CORDIS