Instituts thématiques

Inserm

Institut national
de la santé et de la recherche médicale

Paris, 27 May 2016

Press release

Skin cancer: a team synthesises new drugs with surprising powers

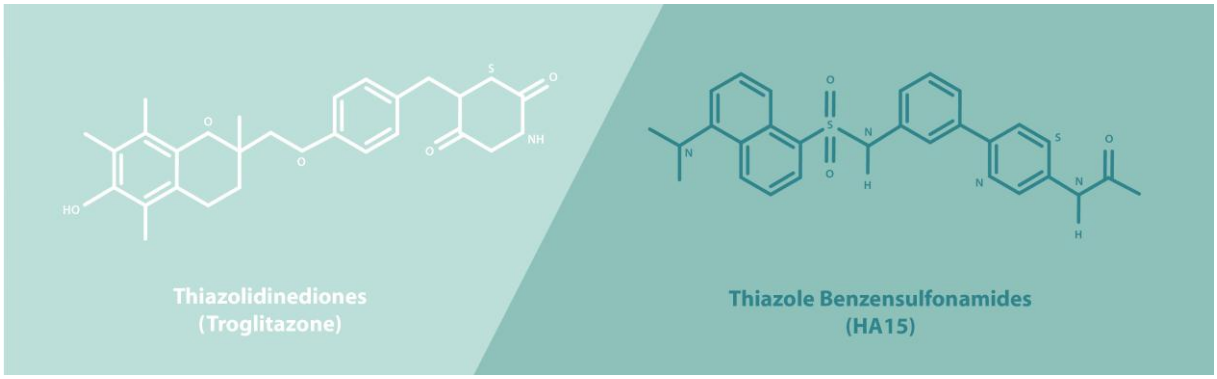
Finding new, more effective and personalised treatments for cancer is the challenge of many researchers. A challenge that has been successfully met by a team from Inserm led by Stéphane Rocchi (Inserm Unit 1065, "Mediterranean Center for Molecular Medicine"), which has just synthesised and developed new drugs for melanoma. One of them, known as HA15, reduces the viability of melanoma cells without being toxic for normal cells. This work has just been published in the journal *Cancer Cell*.

Melanoma is a highly aggressive form of skin cancer. It affects melanocytes, the cells responsible for the synthesis of melanin, which gives the skin its colour. There are 3 stages of tumour progression: radial growth, in which the cells proliferate in a disordered manner in the epidermis, the vertical growth phase, which involves invasion of the dermis, and finally the metastatic phase, corresponding to the dissemination of the cancer cells in the peripheral tissues.

Although encouraging results have been obtained for treating the metastatic phase (using targeted therapies or immunotherapies), most patients will need additional treatments to prevent the tumour from coming back, and to prevent more metastases from developing. The identification of new drug candidates is therefore an unavoidable element for the establishment of effective biotherapies against this cancer, the incidence of which is doubling every ten years.

In this context, researchers from Nice discovered a new family of drugs, the Thiazole Benzensulfonamides (TZB), which have useful anticancer properties. *"Initially this family of drugs was identified in type 2 diabetes, as it increased the sensitivity of cells to insulin. If we wanted to use it against cancer, we had to be able to eliminate this proinsulin activity,"* explains Stéphane Rocchi. *"Thus we started to modify its structure."*

After many attempts, the initial TZD structure was extensively modified thanks to a fruitful collaboration with Dr Benhida's team from the Nice Institute of Chemistry, to obtain a formulation in which the "lead compound" was called HA15.



Their results show that HA15 reduces the viability of melanoma cells without being toxic for normal cells. HA15 induces stress in the endoplasmic reticulum, bringing about the death of the melanoma cells through apoptosis and autophagy.
In the mouse, this drug is highly effective in reducing the tumour volume without obvious toxicity in the rodent.

In humans, in collaboration with the Dermatology Department in Nice University Hospital, the researchers showed that the drugs were active on melanoma cells from biopsies taken from patients who were sensitive or resistant to targeted therapies.

Finally, HA15 is also effective on cell lines from other tumours such as cancer of the breast, colon, prostate, pancreas, and even gliomas and chronic myeloid leukaemias.

"The ultimate goal of this project is to use these new drugs to treat melanoma, and more generally in other types of cancers," concludes Stéphane Rocchi, who hopes to start a phase I clinical trial soon.

This work has been the subject of two 2 patent applications filed by INSERM Transfert and a presentation to the MATWIN programme for technology transfer, and has received funding for maturation from Canceropole PACA and INSERM Transfert (Grand COPOC).

Sources

Compounds triggering endoplasmic reticulum stress exert anti-melanoma effects and overcome BRAF inhibitor resistance.

Michael Cerezo[1,2#], Abdelali Lehraiki[1,2#], Antoine Millet[3#], Florian Rouaud[1,2], Magali Plaisant[1,2], Emilie Jaune[1,2], Thomas Botton[1,2], Cyril Ronco[3], Patricia Abbe[1,2], Hela Amdouni[3], Thierry Passeron[1,2,4],Veronique Hofman[5,6,2], Baharia Mograbi[5,2], Anne-Sophie Dabert-Gay[7,2], Delphine Debayle[7,2], Damien Alcor[1,2], Nabil Rabhi[8] , Jean-Sébastien Annicotte[8] , Laurent Héliot[9], Mariano Gonzalez-Pisfil[9], Caroline Robert[10], Solange Moréra[11], Armelle Virougoux[11], Philippe Gual[12], Maruf MU Ali[13], Corine Bertolotto[1,2,4], Paul Hofman[5,6,2], Robert Ballotti[1,2,4], Rachid Benhida[3*], and Stéphane Rocchi[1,2,4*].

1 INSERM, U1065, Centre Méditerranéen de Médecine Moléculaire (C3M), Equipe Biologie et Pathologie des cellules mélanocytaire : de la pigmentation cutanée au mélanome, Nice, France;
2 Université de Nice Sophia Antipolis, UFR de Médecine, Nice, France;
3 Institut de Chimie de Nice UMR UNS-CNRS 7272, Nice, France;
4 Service de Dermatologie, Hôpital Archet II, CHU Nice, France;
5 Institute of Research on Cancer and Ageing of Nice (IRCAN), INSERM U1081, CNRS UMR7284, Nice, F-06107, France;
6 Laboratoire de pathologie clinique et expérimentale et Hospital-related biobank (BB-0033-00025) , Hôpital Pasteur, Nice, France;
7 Institut de Pharmacologie Moléculaire et Cellulaire (IPMC), CNRS UMR 7275, Sophia Antipolis, France.;
8 Univ. Lille, CNRS, Institut Pasteur de Lille, UMR 8199 - EGID, F-59000 Lille, France;
9 Equipe Biophotonique Cellulaire Fonctionnelle, Laboratoire de Physique des Lasers, Atomes et Molécules (PhLAM) GDR 2588, Villeneuve d'Ascq cedex , France
10 Department of Dermatology, Cancer Campus, Gustave Roussy Institute, Villejuif, France;
11 Institute for Integrative Biology of the Cell (I2BC), CNRS CEA Univ. Paris-Sud, Université Paris-Saclay, Gif-sur-Yvette 91198, France;
12 INSERM, U1065, Centre Méditerranéen de Médecine Moléculaire (C3M), team 8, Nice, France;
13 Department of Life Sciences, Imperial College, London, United Kingdom.

Investigator contact

Stéphane Rocchi
Inserm Research Director
Inserm Unit 1065, "Mediterranean Center for Molecular Medicine" / c3m, Nice
Stephane.rocchi@unice.fr
Tel.: +33 (0)4 89 06 43 33

Press contact

presse@inserm.fr

 Access the Inserm press room