

A program to improve treatment of retinoblastoma

Current treatment of retinoblastoma in France

Retinoblastoma is a cancerous tumor of the eye affecting the cells of the retina. It is quite rare (1 case in 15 000 to 20 000 births), and affects young children, generally before the age of five. Often hereditary, this serious disease affects one eye in 60% of cases, and both eyes in 40% of cases.

The Institut Curie is a reference center in France for the treatment of retinoblastoma, and treats over 60 children every year, ie, about 80% of new cases. 90% of all genetic tests and predisposition testing are done here.

Although diagnosis of retinoblastoma is often relatively simple, it is sometimes made rather late. An ophthalmologic examination should be sought without delay if a child's pupil appears white (instead of orange-red) when light is shined into it, or if a child has strabismus (the eyes appear to look in different directions). Early diagnosis means early treatment, and therefore a better chance of saving both eye and sight. Treatments are increasingly effective, and in the long term 95% of children in the developed world are cured. Various targeted therapies are used to treat each type of tumor specifically. However, the visual prognosis may be compromised depending on the site of the tumor and the impact of treatment on the retina. Larger tumors still require enucleation (surgical removal of the eye).

Developing new, sight-saving treatments

The search for new treatments, and the improvement of existing ones so as to enhance vision preservation, remain a top priority for physicians and researchers at the Institut Curie.

In clinical research, physicians assess new treatment protocols, notably chemotherapy and radiotherapy, which could reduce the risk of vision loss, and secondary cancer.

In their search for genetic predisposition to retinoblastoma, Institut Curie scientists and physicians are seeking to improve detection of mutations in the *RB1* gene that cause retinoblastoma. At the same time, they are investigating whether the type of genetic abnormality in the *RB1* gene is correlated with disease progression (number of tumors, invasive character, occurrence of other tumors in the case of genetic predisposition).

In basic research, efforts are focused on new therapeutic approaches that minimize side effects. Chemotherapy, like radiotherapy, may have more or less long-term consequences for the risk of secondary tumors, and radiotherapy also impacts on the development of the child's facial structure. Dynamic phototherapy, which is based on the activation by visible light of photosensitive molecules, called photosensitizers, is a particularly interesting alternative.

Chemists have developed original photosensitizers from compounds already used clinically for other diseases. In an *in vitro* study of retinoblastoma cells, one hundred or so compounds have

been screened for those that ally efficacy and ease of synthesis. The selected compounds are currently undergoing evaluation for use in tests in *in vivo* models. Biologists are studying the mechanisms underpinning the development of retinoblastoma, since it is essential to understand the stages of carcinogenesis if we are to identify new therapeutic targets.

The Incentive and Cooperative Research Program on Retinoblastoma is a perfect example of multidisciplinary collaboration between physicians, biologists, chemists, and physicists at the Institut Curie.

Incentive and Cooperative Research Program on Retinoblastoma

- Started in January 2006, and scheduled to run for 3 years;
- Funded to the tune of 153 000 euros per year, notably thanks to public donations;
- Coordinators: Philippe Maillard, CNRS Junior Director of Research in the Design, Synthesis and Targeting of Biomolecules team, UMR 176 CNRS/Institut Curie Research Center, and Prof François Doz, a pediatrician in the Pediatric Oncology Department of the Institut Curie Hospital;
- Seven research projects are being run in three thematics (fundamental biology, genetics, experimental treatments) by 19 scientists (physicians or researchers) at the Institut Curie, plus external collaborators.

