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Common cause of miscarriage, cancer and Down syndrome – 108th International Titisee Conference

If a cell gains or loses large parts of its genetic material or even whole chromosomes, it is termed aneuploidy. In body cells, it can cause cancer; in eggs or sperm miscarriages or disorders such as Down syndrome can ensue. At the 108th International Titisee Conference (ITC) “Causes and consequences of aneuploidy”, world leading researchers will discuss the rapid progress currently being made in understanding the processes that result in aneuploidy and how this state affects cells. The conference, organized by the Boehringer Ingelheim Fonds, is chaired by Prof. Angelika Amon and takes place from October 24-27, 2013 on the shores of Lake Titisee in Germany.

The genetic material (or DNA) of most organisms is packaged into a number of so-called chromosomes. Before division, a cell copies its DNA to equip both its daughter cells with the appropriate number of chromosomes. Aneuploidy mostly arises as a result of mistakes during this distribution of DNA, leading to daughter cells that have gained or lost large parts of or even whole chromosomes. If this occurs in sperm or eggs, all cells of the resulting organism are affected. Such whole-body aneuploidy is the most common cause of miscarriage and mental retardation in humans. Aneuploidy is also associated with cancer. About 90 per cent of all solid tumours and about 75 per cent of all blood cancers have gained or lost entire chromosomes. How aneuploidy contributes to tumourigenesis is a critical question that is not yet completely understood and will be discussed during the conference.

For the development of a healthy organism, all genes as well as their protein products, must be carefully regulated. “If one copy of a single gene has been lost or gained, the cell and therefore a developing embryo often have ways of coping with it. But if – as happens in aneuploidy – a large number of proteins are affected, cells are in trouble,” explains Angelika Amon from the Massachusetts Institute of Technology (MIT) in Cambridge USA and Chair of the 108th ITC. “It is easy to see why missing proteins or too low a concentration are a problem for a cell – it lacks the tools to carry out vital functions. But too much of a whole number of proteins is just as bad: they upset the delicate balance of the different proteins and gene-regulation factors, choke the cell’s folding and degradation pathways, or interfere with other proteins by binding with their reaction partners. Because of the dramatic impact that gaining or losing a chromosomes has on cells, it is critical that we understand the mechanisms underlying their faithful segregation during cell division.”

The 108th ITC will bring together leading researchers who study how chromosomes are distributed between daughter cells. Research into the occurrence of aneuploidy and its effects on cells has led to
hypothses as to how chromosome mis-segregation and the ensuing aneuploidy contributes to carcinogenesis. The recent development of mouse models of aneuploidy will now enable these hypothses to be tested and should provide not only fundamental insights into tumour evolution but will also set the stage for the development of therapeutics that target the aneuploid state in cancer. “Recently, we have gained dramatic new insights into the mechanisms governing chromosome segregation. We have uncovered new possibilities of studying them in mouse models, opening ways for a better understanding of aneuploidy-related diseases like cancer,” says Prof. Don. W. Cleveland from the Ludwig Institute for Cancer Research at the University of California, San Diego, USA and co-chair of the conference.

**Whole-body versus mosaic aneuploidy**

Whole-body aneuploidy, in which all body cells are affected, is the more severe form: the loss of any chromosome – apart from second sex chromosome X or Y – is always lethal for the foetus. The gain of a chromosome is known as trisomy and Down syndrome or trisomy 21, develops if a foetus has three copies of chromosome 21 instead of the normal two. Of all the whole-body trisomies, only children with trisomy 21 or an abnormal number of the sex chromosomes survive to adulthood. If aneuploidy arises later in foetal development or after birth, it affects only a subset of the body’s cells and is termed mosaic aneuploidy. This condition also disrupts foetal development and often leads to the same problems as whole-body aneuploidy, depending on the number of cells involved.

**108th ITC – still going strong**

The International Titisee Conferences of the Boehringer Ingelheim Fonds (BIF) started out in 1962 with a concept that still proves attractive today. “Take a beautiful setting, bring together a limited number of leading scientists from two to three different sub disciplines, who normally would not meet, then give them three days’ time away from the bustle of their lab to find new ways of looking at things and start new co-operations to push the field ahead,” says Dr Claudia Walther, Managing Director of the BIF. Participation is by invitation only, and the maximum number of attendees is around 60. All participants are requested to stay for the duration of the meeting to allow ample time for discussion and the fostering of new collaborations. The scientists on the Board of Trustees of BIF select chairs and topics and BIF itself takes care of all the financial and organizational details. The chairs only need to narrow down the topic and decide, whom they wish to invite. “I am proud to have been selected to chair one of these prestigious meetings,” states Angelika Amon, “and I am looking forward to a relaxed atmosphere in which we expect to develop exciting new ideas. With every bit of understanding, we come closer to finding effective treatments against the many diseases related to aneuploidy.”

The **International Titisee Conferences** (ITCs) have been held at Lake Titisee, in the attractive surroundings of the Black Forest in southern Germany since 1962. Their topics cover the entire spectrum of basic research in biomedicine, ranging from “The dynamical brain” to “Protein design at the crossroads of biotechnology, chemistry, and evolution”. Since 1983, these twice-yearly conferences have been funded and organized by the **Boehringer Ingelheim Fonds** (BIF), an independent public foundation for the promotion of basic research in medicine. The BIF also awards international PhD and MD fellowships for up-and-coming scientists as well as travel grants for PhD and postdoctoral fellows ([www.bifonds.de](http://www.bifonds.de)).
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