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Updates in preserving reproductive potential of pre-pubertal girls with cancer

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Which increasing numbers of adult female survivors of childhood cancers due to advances in early diagnosis and treatment, the issue of preserving the reproductive potential of prepubertal girls undergoing gonadotoxic treatments has gained greater attention. Unfortunately, the two established fertility preservation options, embryo freezing and egg freezing, cannot be offered routinely to prepubertal girls as these options necessitate prior ovarian stimulation and subsequent mature oocytes retrieval that are contraindicated or infeasible before puberty. Therefore, the most suitable fertility preservation options to prepubertal girls are (1) ovarian tissue freezing and autotransplantation, (2) *in vitro* maturation, and (3) ovarian protection techniques. In this presentation, those fertility preservation options as well as their success rates, advantages, disadvantages and future directions will be discussed in detail. Also a new integrated strategy to preserve the reproductive potential of prepubertal girls with cancer will be highlighted. Although experimental, ovarian tissue slow freezing and orthotopic autotransplantation may be the most feasible option to preserve the reproductive potential of prepubertal girls with cancer. However, this technique has two major and serious disadvantages: (1) the risk of reintroducing malignant cells and (2) the relatively short lifespan of ovarian tissue transplants. Several medical and ethical considerations should be taken into account before applying this technique to prepubertal girls with cancer.

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Novel treatment options against minimal residual disease in children using a preclinical model of acute leukemia

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While first line poly-chemotherapy substantially reduces tumor burden in most children with acute leukemia, a subgroup of children retain residual tumor cells in a disease stage called minimal residual disease (MRD). Despite low tumor burden, MRD represents a major threat as it consists of treatment resistant cells which might induce disease relapse with inferior prognosis. Novel treatment options are urgently required to treat children with acute leukemia at MRD. We aimed at the preclinical testing novel treatment options for MRD. Towards this aim, we established the individualized mouse model of acute leukemias and transplanted primary tumor cells from children with either Acute Lymphoblastic Leukemia (ALL) or Acute Myloid Leukemia (AML) into severely immunocompromised mice and generated patient-derived xenograft cells thereof. Using lenti-viral transduction, we molecularly marked patient-derived xenograft cells with luciferase allowing highly sensitive and reliable bioluminescence *in vivo* imaging in single mice over time. Imaging allowed establishing a mouse model of MRD using conventional poly-chemotherapy consisting of an anthracycline combined with Cytarabine in AML and a 3 drug poly-chemotherapy for ALL. Using enrichment strategies based on the expression of additional trans-genes, we re-isolated MRD cells from mice and performed single cell RNA sequencing to characterize the cells. We performed second line treatment starting at the disease stage of MRD. Our model allows characterizing MRD cells in more detail and testing novel treatment options to remove MRD cells in order to prevent disease relapse and to improve the prognosis of children with acute leukemias.

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