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Communicating about illness: family nursing in oncology care

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Cancer nursing includes not just assisting the patients but also their families to adjust and adapt to a life with cancer. The impact of both the illness and its treatment require individuals and their families to make changes to their lifestyles [1]. Cancer nursing practice is based on the notion of holism which includes the acceptance of cancer as a 'family illness' [2]. Also palliative care, which is often part of oncology care, emphasize the family in its definition 'the goal of palliative care is achievement of the best possible quality of life for patients and their families' [3]. The home is increasingly seen as the ideal place to dwell, even when ill, and a trend is that responsibility for the care of the ill will shift from the public sector to the family [4]. It has been suggested that family nursing enables nurses to work with the family in a supportive and more purposeful way, and family care has even been suggested to replace that of individual care [5]. Traditionally, the focus of nursing has been on the practice of nursing with individual patients [6]. If nurses involve families more in care, they need to modify their usual pattern of clinical practice [7]. Family nursing has evolved as a way of thinking about and working with families. Family nursing comprises a philosophy and a way of interacting with individuals and families that affect how nurses collect information, intervene with and advocate for patients/families [6]. For the family to have a chance to talk about issues such as hope and suffering in palliative care, both within the family and with the nurses, has been shown to be a healing experience. It gave them the opportunity to unburden themselves, as well as a way of learning and finding new strategies for managing daily life [8]. Family nursing could be an intervention where patients with cancer and their families are supported in identifying their own strengths and resources and also needs that require external resources [9]. This presentation will reflect on family nursing in oncology care.

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Scientific Symposium (Tue, 22 Sep, 14:45−16:45)
The DNA damage response in cancer: role in tumourigenesis and targeted therapy

155 INVITED

SMARCA5 links chromatin remodeling with the DNA damage response

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Our genome is faced with DNA damage induced by endogenous (e.g. free radicals) and exogenous sources (e.g. ionizing radiation). Failure to repair DNA damage can lead to genomic instability, cancer development or cell death. Efficient repair of DNA lesions, however, is complicated by the fact that genomic DNA is packaged, through histone and non-histone proteins, into a condensed structure called chromatin. The DNA repair machinery has to circumvent this natural barrier to gain access to damaged DNA and repair DNA lesions. Our recent work in budding yeast demonstrated that ATP-dependent chromatin remodeling is a mechanism that cells use to alter chromatin structure at DNA lesions and promote DNA repair. However, the role of chromatin remodeling during DNA repair in mammalian cells remained largely unexplored. We performed a genome-wide RNA interference screen in the nematode *C.elegans* and identified *isw-1,* a SWI/SNF2-related chromatin remodeling factor, as a potential novel regulator of the DNA damage response. The human homologue of ISW-1*,* SMARCA5, rapidly accumulates at sites of laser-induced DNA damage, an event that is followed by the accumulation of different DNA damage response factors. Knockdown of SMARCA5 impaired the accumulation of these factors at sites of DNA damage, caused defects in checkpoint activation and DNA repair, and rendered cells hypersensitive to ionizing radiation. These results suggest that SMARCA5 chromatin remodeling protects genome integrity by modulating chromatin structure at DNA lesions to orchestrate the recruitment of DNA damage response factors. Moreover, SMARCA5 dysfunction may contribute to cancer development as defects in the DNA damage response have been linked to a number of genomic instability syndromes that are characterized by cancer predisposition.

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Exploiting cancer defects in targeted therapy

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DNA repair and damage response pathways are activated as a tumour barrier at early stages during cancer development. Here, we show that oncogene-induced senescence is associated with signs of DNA replication stress, including prematurely terminated DNA replication forks and DNA double strand breaks. A new concept for cancer therapy is to amplify endogenous tumour-specific DNA lesions, to specifically kill tumour cells. Based on this concept we report that BRCA2 defective breast cancers can be specifically targeted using inhibitors of Poly(ADP-ribose) polymerase (PARP). We show that BRCA2 deficient cells, as a result of their recombination deficiency, are acutely sensitive to PARP inhibitors, presumably because resultant collapsed forks are no longer repaired. We exploit this requirement to specifically kill BRCA2 deficient tumours by PARP inhibition alone.
If replication forks stall, a multifaceted response including several DNA repair and cell cycle checkpoint pathways is activated to ensure faithful DNA replication. Here, we show that PARP1 binds to and is activated by stalled replication forks. PARP1 collaborates with Mre11 to promote replication fork restart following release from replication blocks, likely through Mre11-mediated resection of DNA. Both PARP1 and PARP2 are required for subsequent homologous recombination to promote cell survival following replication blocks. Our data suggest that PARP1 and PARP2 act as sensors of replication stress and are required for Mre11-mediated restart and recombination repair of stalled replication forks.

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Repair DNA polymerases as anticancer drug targets

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Mammalian genomes are large and complex, thus requiring tightly regulated and coordinated processes to maintain the integrity of the genetic information, such as DNA replication, DNA repair, translesion DNA synthesis, involving the activity of multiple DNA polymerases (DNA pols). Several different DNA pols with different enzymatic properties (processivity, fidelity, substrate specificity) are acting in mammalian cells. Significant functional redundancy exists among certain DNA pols, while others appear to have unique functional roles. These enzymes are the only biological macromolecules able to duplicate the genetic information stored in the DNA and are absolutely required every time this information has to be copied, as during DNA replication or during DNA repair, when lost or damaged DNA sequences have to be replaced with "original" or "correct" copies. In each DNA repair pathway one or more specific DNA pols are required. A feature of mammalian DNA repair pathways is their redundancy. The failure of one of these pathways can be compensated by another one. However, several DNA lesions require a specific repair pathway for error free repair. In many tumors one or more DNA repair pathways are affected, leading to error prone repair of some kind of lesions by alternatives routes, causing accumulation of mutations and contributing to genomic instability, a common feauture of cancer cells. An overview of the different DNA pols