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About UICC
The Union for International Cancer Control (UICC) is the leading international non-governmental organization dedicated to global cancer control.

Founded in 1933, UICC unites over 300 member organizations, specialized and engaged in cancer control, in more than 100 countries across the world.

UICC’s mission is to connect, mobilize and support organizations, leading experts, key stakeholders and volunteers in a dynamic community working together to eliminate cancer as a life-threatening disease for future generations.

UICC works closely with its member organizations and partners to implement a comprehensive strategy that includes
- promoting the World Cancer Declaration
- organizing the World Cancer Congress
- raising awareness through the World Cancer Campaign
- coordinating World Cancer Day annually, on 4 February
- reviewing and disseminating the TNM (tumour-node-metastasis) classification of malignant tumours
- developing effective cancer control programmes especially in low- and middle-income countries

- changing cancer-related beliefs and behaviour through information and education
- creating special initiatives in prevention, early detection, access to treatment and supportive care
- awarding international cancer fellowships
- producing cutting-edge scientific publications, such as the International Journal of Cancer

UICC is governed by its member organizations, which meet in a general assembly, held in conjunction with the World Cancer Congress, every two years. Between assemblies, a board of 17 directors, elected by the general assembly, acts as the executive body of the UICC.

UICC works closely with the World Health Organization (WHO), the International Agency for Research on Cancer (IARC), and the Programme of Action for Cancer Therapy (PACT) and has consultative status with the UN Economic and Social Council. It offers corporate partners a unique opportunity to demonstrate social responsibility on a global scale. Every two years.

UICC is non-profit, non-political and non-sectarian. Its headquarters are in Geneva, Switzerland. www.uicc.org
Species-specific role of gene-adjacent retroelements in human and mouse gastric carcinogenesis
Mun-Gan Rhyu, Jung-Hwan Oh, and Seung-Jin Hong

Generational shift in melanoma incidence and mortality in Queensland, Australia, 1995–2014
Joanne F. Aitken, Danny R. Youlden, Peter D. Baade, H. Peter Soyer, Adèle C. Green, and B. Mark Smithers
Queensland, Australia has long had the highest recorded melanoma incidence in the world, with public campaigns encouraging sun protection for skin cancer prevention beginning in the early 1980s. Here, the authors examined recent trends to assess whether earlier evidence of stabilizing melanoma incidence in young people has persisted. They show that rates of invasive melanoma have peaked over the last two decades for persons aged under 60. Coupled with stable or declining mortality rates, except in men over 60, the results provide substantive evidence that long-running melanoma prevention and early-detection campaigns have reduced the burden of melanoma across successive generations.

Personal history of non-melanoma skin cancer diagnosis and death from melanoma in women
Steven T. Chen, Xin Li, and Jiali Han
As melanoma incidence climbs, prevention and early detection are becoming increasingly important. Here, the effect of personal history of non-melanoma skin cancer (NMSC) on risk of melanoma diagnosis and death was examined among women enrolled in the Nurses’ Health Study between 1986 and 2012. Women with history of NMSC were found to be more likely to develop non-lethal melanoma than lethal disease and to have slightly reduced risk of advanced melanoma and death. Overall, however, history of NMSC was associated with increased risk of melanoma diagnosis, suggesting that vigilance in melanoma detection after NMSC diagnosis could lessen disease burden.

Life course evolution of body size and breast cancer survival in the E3N cohort
Mathilde His, Marine Le Guenlec, Sylvie Mesrine, Marie-Christine Boutron-Ruault, Françoise Clavel-Chapelon, Guy Fagherazzi, and Laure Dossus
Obesity is a known factor affecting breast cancer survival. It remains unclear, however, whether body size in early life is associated with breast cancer survival in adulthood, or whether only adult obesity is relevant in this context. Here, analyses of life-course body size from childhood through puberty to adulthood show that an increase in body silhouette, particularly during adulthood, is associated with elevated risks of breast cancer recurrence, second primary cancer and death. The findings suggest that consideration of body size trajectory can help identify breast cancer survivors with increased likelihood of recurrence and poor outcome.

Waist circumference and risk of breast cancer in Korean women: A nationwide cohort study
Kyu Rae Lee, In Cheol Hwang, Kyung Do Han, Jinyung Jung, and Mi Hae Seo
While excess body fat is a risk factor for postmenopausal breast cancer, whether a similar link exists between adiposity and premenopausal breast cancer risk remains uncertain. Here, among Korean women, both body mass index (BMI) and waist circumference were strongly associated with postmenopausal breast cancer risk. BMI was inversely associated with premenopausal breast cancer risk. In all women, BMI adjustment modified associations between waist circumference and breast cancer risk. The findings suggest that unlike postmenopausal breast cancer, where general and central obesity independently predict risk, premenopausal breast cancer risk is predicted by central obesity only when general adiposity is considered.
Interaction between tobacco smoking and hepatitis B virus infection on the risk of liver cancer in a Chinese population

Xing Liu, Aileen Baecker, Ming Wu, Jin-Yi Zhou, Jie Yang, Ren-Qiang Han, Pei-Hua Wang, Zi-Yi Jin, Al-Min Liu, Xiaoping Gu, Xiao-Feng Zhang, Xu-Shan Wang, Ming Su, Xu Hu, Zheng Sun, Gang Li, Lina Mu, Na He, Liming Li, Jin-Kou Zhao, and Zuo-Feng Zhang

Tobacco smoking is a major risk factor for various cancer types, including liver cancer. Half of new liver cancer cases reported annually worldwide occur in China, where the prevalence of smoking and hepatitis B virus (HBV) infection are high. Here, associations between tobacco smoking and liver cancer and interactions between smoking and other risk factors were examined in a Chinese population. Significant interactions were detected between smoking and HBV infection. Analyses by gender indicated that associations between smoking and liver cancer existed primarily among men, who were more likely than women to have been ever smokers or current smokers.

Drivers of advanced stage at breast cancer diagnosis in the multicountry African breast cancer – disparities in outcomes (ABC-DO) study

Fiona McKenzie, Annelle Zietsman, Moses Galukande, Angelica Anele, Charles Adisa, Groesbeck Parham, Leeya Pinder, Herbert Cubasch, Maureen Joffe, Frederick Kidaaga, Robert Lukande, Awa U. Offlah, Ralph O. Egjeru, Aaron Shibemba, Joachim Schuz, Benjamin O. Anderson, Isabel dos Santos Silva, and Valerie McCormack

Breast cancer (BC) patients in sub-Saharan Africa (SSA) tend to have poor prognoses and low survival rates. This is largely because the majority of cases are not diagnosed until the disease has reached an advanced stage. In this study, the authors found that delayed diagnosis is associated with several modifiable factors, including limited schooling, low-wage jobs, and lack of awareness of BC. With incidence rates of BC steadily climbing in SSA, it is urgent that efforts to improve disease-specific education and awareness both among women and throughout the healthcare system be intensified.

Acne in late adolescence and risk of prostate cancer

Henrik Ugge, Ruzan Udumyan, Jessica Carlsson, Ove Andrén, Scott Montgomery, Sabina Davidsson, and Katja Fall

Some evidence has suggested that acne vulgaris may increase the risk of prostate cancer, but the data have been inconsistent. The results of this prospective cohort study support a link between acne in adolescence and prostate cancer later in life, potentially implicating the bacteria Propionibacterium acnes and resulting inflammation in prostate carcinogenesis. These results also suggest that the association may be stronger for the most severe type of acne and for advanced prostate cancer.

Trends in incidence, mortality and survival of penile squamous cell carcinoma in Norway 1956–2015

Bo T. Hansen, Madleen Orumaa, A. Kathrine Lie, Bjørn Brennhovd, and Mari Nygård

Current trends in penile cancer incidence are unclear. Some studies suggest that the disease is on the rise, while others indicate the opposite. Our study examined changes in penile squamous cell carcinoma (SCC) incidence in Norway from 1956 to 2015. The results show that penile SCC incidence climbed steadily over the 60-year period, especially among younger men. Mortality associated with penile PCC rose somewhat, while survival did not change significantly, indicating that changes in treatment have only marginally benefited survival. The observed increase in incidence may be associated with increased human papillomavirus (HPV) transmission, which is preventable through HPV vaccination.

Genome-wide association study identifies the GLDC/IL33 locus associated with survival of osteosarcoma patients

Roelof Koster, Orestis A. Panagiotou, William A. Wheeler, Eric Karlins, Julie M. Gastier-Foster, Silvia Regina Caminada de Toledo, Antonio S. Petrelli, Adrienne M. Flanagan, Roberto Tirabosco, Irene L. Andrilis, Jay S. Wunder, Nalan Gokgoz, Ana Patiño-Garcia, Fernando Lecanda, Massimo Serra, Claudia Hattinger, Piero Picci, Katia Scotlandi, David M. Thomas, Mandy L. Ballinger, Richard Gorlick, Donald A. Barkauskas, Logan G. Spector, Margaret Tucker, D. Hicks Belynda, Meredith Yeager, Robert N. Hoover, Sholom Wacholder, Stephen J. Chanock, Sharon A. Savage, and Lisa Mirabello

To date, prognostic factors associated with survival in patients with osteosarcoma are scarce. Here, the authors conducted a multi-institutional-genome-wide association study to explore whether germline genetics may contribute to overall survival in osteosarcoma patients. They identified a common single nucleotide polymorphism, rs55933544, located in the GLDC gene on chromosome 9, associated with poor survival. The rs55933544 risk allele was associated with lower expression of the nearby gene, IL33. These findings, if replicated in additional populations, form the foundation for future studies of the molecular basis of the association of the GLDC/IL33 (rs55933544) variant with survival in osteosarcoma.
Integrating expression-related SNPs into genome-wide gene- and pathway-based analyses identified novel lung cancer susceptibility genes

Yuzhuo Wang, Weibing Wu, Meng Zhu, Cheng Wang, Wei Shen, Yang Cheng, Liguo Geng, Zhihua Li, Jiahui Zhang, Juncheng Dai, Hongxia Ma, Liang Chen, Zhibin Hu, Guangfu Jin, and Hongbing Shen

Single nucleotide polymorphisms (SNPs) can be mapped to genes based on physical position, though this approach may overlook biologically relevant aspects of SNPs. In our study, information from gene expression was integrated with gene- and pathway-based analyses to discover genetic variants and pathways linked to lung cancer. While four lung cancer susceptibility loci were validated and three new lung cancer susceptibility genes identified using gene-based analysis, pathway-analysis led to the discovery of nine pathways associated with lung cancer risk. The findings suggest that integration of expression-related SNPs with genome-wide analytical approaches can facilitate the discovery of disease-associated genes and mechanisms.

DNA methylation-based biological aging and cancer risk and survival: Pooled analysis of seven prospective studies

Pierre-Antoine Dugué, Julie K. Bassett, JiHoon E. Joo, Chol-Hee Jung, Ee Ming Wong, Margarita Moreno-Betancur, Daniel Schmidt, Enes Makalic, Shuai Li, Gianluca Severi, Allison M. Hodge, Daniel D. Buchanan, Dallas R. English, John L. Hopper, Melissa C. Southey, Graham G. Giles, and Roger L. Milne

Aging is associated with profound changes in DNA methylation levels. These can be used to build accurate age predictors ("epigenetic clocks") that deviate from chronological age by only a few years, a phenomenon named "age acceleration". In this study of seven types of cancer, the authors found that age acceleration was associated with both increased cancer risk and decreased cancer survival, independently of major health risk factors. These results support the usefulness of methylation markers of biological aging as a tool to predict health outcomes and may provide valuable insight into the relationship between aging and cancer.

How to analyse the spatiotemporal tumour samples needed to investigate cancer evolution: A case study using paired primary and recurrent glioblastoma

Alastair Droop, Alexander Bruns, Georgette Tanner, Nora Rippaus, Ruth Morton, Sally Harrison, Henry King, Katherine Ashton, Khaja Syed, Michael D. Jenkinson, Andrew Brodbelt, Aruna Chakrabarty, Azzam Ismail, Susan Short, and Lucy F. Stead

Tumor evolution, in which selection favors the survival of genetically and phenotypically distinct subclones, is a key feature of cancer progression. Within a single patient, such subclones may be shared across multiple tumors and carry somatic mutations that facilitate cancerous driver events. Here, an adapted two-stage approach to mutation calling was used to identify shared somatic mutations across multiple matched tumors from the same patient. The approach showed high sensitivity in the detection of shared genetic variants in analyses of paired primary and recurrent glioblastoma samples, suggesting that it could potentially improve the capture of biologically relevant somatic mutations.

Identification of a novel fusion gene HMGA2-EGFR in glioblastoma

Akiyoshi Komuro, Ema Raja, Caname Iwata, Manabu Soda, Kazunobu Isogaya, Keiko Yuki, Yasushi Ino, Masato Morikawa, Tomoki Todo, Hiroyuki Aburatani, Hiromichi Suzuki, Melissa Ranjit, Atsushi Natsume, Akitake Mukasa, Nobuhito Saito, Hitoshi Okada, Hiroyuki Mano, Kohei Miyazono, and Daizo Koinuma

Fusion genes are promising targets for the development of novel drug therapies against glioblastoma. Little is known, however, about their role in the disease. Here, a novel fusion gene, HMGA2-EGFR, was identified from a human glioblastoma specimen containing glioma-initiating cells (GICs). Forced expression of the HMGA2-EGFR fusion protein induced transformation of NIH3T3 fibroblasts and, in glioblastoma cells, induced STAT5B phosphorylation, similar to the known EGFR mutant EGFRvIII. HMGA2-EGFR overexpression also accelerated the growth of orthotopic U87MG tumors in mice, while the EGFR inhibitor erlotinib suppressed tumor formation by HMGA2-EGFR-expressing GICs and prolonged the survival of tumor-bearing mice.
Truncated isoform Vav3.1 is highly expressed in ovarian cancer stem cells and clinically relevant in predicting prognosis and platinum-response
Daniel Reimer, Maximilian Boesch, Dominik Wolf, Christian Marth, Sieghart Sopper, Jiri Hatina, Peter Altevogt, Walther Parson, Hubert Hackl, and Alain G. Zeimet

Ovarian cancer is the most lethal gynecologic cancer in Western countries. Platinum resistance is a major obstacle for sufficient treatment, though understanding of the mechanisms involved in platinum resistance is incomplete. Our study shows that the N-terminal truncated Vav3.1 isoform, produced by alternative splicing of Vav3, a modulator of GTP hydrolases of the Rho/Rac family, is overexpressed in multi-drug resistant stem-cell like fractions of ovarian cancer cells. Vav3.1 expression was significantly higher in platinum-refractory ovarian cancers compared to other ovarian cancer specimens, with marked overexpression in ovarian tumors with genuine but not acquired platinum resistance.

Ezrin mediates both HGF/Met autocrine and non-autocrine signaling-induced metastasis in melanoma
Liping Huang, Yifei Qin, Qiang Zuo, Kavita Bhatnagar, Jingbo Xiong, Glenn Merlino, and Yanlin Yu

Aberrant HGF/Met signaling promotes tumor migration, invasion, and metastasis through autocrine and non-autocrine mechanisms; however, the molecular downstream signaling mechanisms by which HGF/Met induces metastasis remain unclear. Our study provides evidence that the cytoskeletal organizer Ezrin is a key downstream factor involved in the regulation of HGF/Met signaling-induced metastasis and demonstrates a link between Ezrin and HGF/Met/MAPK/Sp1 activation in the metastatic process. The finding that Ezrin is located downstream of HGF/Met signaling helps explain the high metastatic potential long associated with the Met receptor and highlights Ezrin as a promising therapeutic target for patients bearing tumors with activated HGF/Met signaling.

Prognostic utility of six mutated genes for older patients with acute myeloid leukemia
Jinghan Wang, Zhixin Ma, Qinrong Wang, Qi Guo, Jiansong Huang, Wenjuan Yu, Huanping Wang, Jingwen Huang, Yang Washington Shao, Suning Chen, and Jie Jin

Overall survival for older patients with acute myeloid leukemia (AML) is generally poor. Certain genetic mutations are correlated with prognosis in younger patients; however, it is not known whether these associations also apply to elderly patients. In our study, the authors identified and validated a pattern of specific mutations that are associated with prognosis in elderly patients, including those of Asian origin. They then developed a precise and simple nomogram to translate these molecular and clinical data into a reliable prediction model for stratifying risk for these patients.

Biweekly cisplatin and gemcitabine in patients with advanced biliary tract cancer
Daniel H. Ahn, Josh Reardon, Chul W. Ahn, Manojkumar Bupathi, Sameh Mikhail, Christina Sing-Ying Wu, and Tanios Bekaii-Saab

Patients diagnosed with biliary tract cancer frequently present with advanced or metastatic disease, for which standard treatment entails an eight-week-long course of weekly administration of combined gemcitabine-cisplatin (GC) chemotherapy. Here, a modified biweekly regimen of GC chemotherapy was examined as a means of potentiily optimizing treatment for advanced biliary cancer. Despite a prolonged treatment course, with a median of six biweekly treatment cycles, the modified regimen was associated with minimal toxicities. Median overall survival was just over 10 months. The findings suggest that biweekly GC administration can reduce treatment-related toxicities, while maintaining clinical efficacy and allowing for continued treatment.

Bevacizumab in combination with different platinum-based doublets in the first-line treatment for advanced nonsquamous non-small-cell lung cancer: A network meta-analysis
Shen Zhao, Fangfang Gao, Yaxiong Zhang, Zhonghan Zhang, and Li Zhang

Patients with untreated advanced nonsquamous non-small-cell lung cancer (NS-NSCLC) typically are treated with a combination of platinum (Pt) and a second chemotherapeutic drug. Bevacizumab may be added to the doublet regimen, though whether its use is beneficial remains unclear. Here, in a meta-analysis of published trials involving NSCLC patients, bevacizumab combined with Pt-carboplatin (Taxane–Pt) was found to confer a significant survival advantage, while gemcitabine–Pt (Gem–Pt) plus bevacizumab showed no benefit over other treatments. Pemetrexed–Pt (Pem–Pt) plus bevacizumab and Pem–Pt had similar efficacy and tolerability. Pem–Pt and Taxane–Pt plus bevacizumab exhibited the best benefit-risk ratios for the study population.
Polymethoxyflavones prevent benzo[a]pyrene/dextran sodium sulfate-induced colorectal carcinogenesis through modulating xenobiotic metabolism and ameliorate autophagic defect in ICR mice

Jia-Ching Wu, Mei-Ling Tsai, Ching-Shu Lai, Chih-Yu Lo, Chi-Tang Ho, Ying-Jan Wang, and Min-Hsiung Pan

Carcinogenic polycyclic aromatic hydrocarbons (PAHs) are pervasive in the environment and are a potential source of food contamination, with their ingestion via dietary sources greatly increasing colorectal cancer (CRC) risk. This study examined the possibility of preventing CRC induced by intake of the PAH benzo[a]pyrene (BaP) via administration of polymethoxyflavones (PMFs), anticancer substances found in citrus peels. The results show that colon tumorigenesis induced by BaP and dextran sulfate sodium (DSS) in mice can be blocked by PMFs oral administration. PMFs were associated with reduced mutagenic metabolite levels and DNA adduct formation and with alleviation of a BaP/DSS-induced autophagic defect.

Inhibition of MK2 suppresses IL-1β, IL-6, and TNF-α-dependent colorectal cancer growth

Anita L. Ray, Kiersten L. Berggren, Sebastian Restrepo Cruz, Gregory N. Gan, and Ellen J. Beswick

The mitogen-activated protein kinase (MAPK) pathway plays a critical role in the development and progression of colorectal cancer (CRC). A key mediator of inflammation in CRC pathogenesis is MAPK-activated protein kinase 2 (MK2). This study examined the impact of MK2 inhibition on inflammation and tumor burden in spontaneous and colitis-associated CRC mouse models. In both models, MK2 served important signaling functions during CRC progression. MK2 inhibition resulted in tumor regression and reductions in tumor burden via cytokine-dependent mechanisms. The findings suggest that MK2 is a potential therapeutic target, with its inhibition leading to decreased cytokine production and tumor growth.

Sodium glucose cotransporter 2 inhibitor canagliflozin attenuates liver cancer cell growth and angiogenic activity by inhibiting glucose uptake

Kosuke Kaji, Norihisa Nishimura, Kenichiro Seki, Shinya Sato, Soichiro Saikawa, Keisuke Nakanishi, Masanori Furukawa, Hideto Kawarata, Mitsuteru Kitade, Kei Moriya, Tadashi Namisaki, and Hitoshi Yoshiji

Sodium-glucose cotransporter 2 inhibitors (SGLT2-Is) comprise a new class of antidiabetic agents that inhibit glucose reabsorption in the renal proximal tubules. Although recent evidence suggests that SGLT2-Is can attenuate growth of SGLT2-expressing cancer cells, little is known about their effects on hepatocellular carcinoma (HCC). Our study shows that the SGLT2-1 canagliflozin directly inhibits the growth of SGLT2-expressing liver cancers by reducing glucose uptake and inhibiting glycolytic metabolism. Furthermore, canagliflozin attenuates proangiogenic activity in SGLT2-expressing liver cancers. Because SGLT2-Is are already used extensively without serious side effects, these agents may emerge as a new therapeutic strategy for HCC patients.

Light therapy and mood in breast cancer

Sara Dallaspezia, Sara Cantamessa, and Francesco Benedetti

Letter to the Editor

Erratum

Corrigendum

Cover Illustration: This photo depicts co-location status of LC3B (green) and LAMP-1 (red) in colonic tissue. BaP/DSS significantly induce autophagic defect via decreased autophagosome-lysosome fusion (yellow) that was improved by pretreatment with PMFs. See the related article by Wu et al., pages 1689–1701.