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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
10 Curcumin analogs: Their roles in pancreatic cancer growth and metastasis
Ganji Purnachandra Nagaraju, Leah Benton, Shipra Reddy Bethi, Mamoru Shoji, and Bassel F. El-Rayes

20 Respiratory morbidity in young people surviving cancer: Population-based study of hospital admissions, treatment-related risk factors and subsequent mortality
Lesley Smith, Adam W. Glaser, Daniel Peckham, Darren C. Greenwood, and Richard G. Feltbower

While survival among victims of childhood cancer has improved significantly in recent decades, delayed effects of treatment remain major causes of late morbidity and mortality. The authors of the present study analyzed factors related to the development of respiratory conditions in survivors originally diagnosed with cancer between ages 0 and 29. Risk of hospitalization from respiratory disease was significantly higher in cancer survivors compared to the general population. In particular, pulmonary toxic chemotherapy was associated with an increased risk of admissions for all respiratory disease, especially pneumonia. Mortality from respiratory disease was highest among survivors admitted for pneumonia.

29 Psychological effect of cervical cancer screening when changing primary screening method from cytology to high-risk human papilloma virus testing
Trude Andreassen, Bo T. Hansen, Birgit Engesæter, Dana Hashim, Nathalie C. Søer, Ameli Tropé, Kåre Moen, Giske Ursin, and Elisabete Weiderpass

Norway is one of the first countries to implement high-risk human papilloma virus (hrHPV) testing in primary cervical-cancer screening. Does this newer type of testing impact the emotional well-being of patients? In this study, the authors found no significant difference in either anxiety or depression scores between the viral-screening arm and standard cytology screening. These findings could be useful for other countries considering implementing hrHPV testing, and are reassuring for the ongoing implementation process in Norway.

40 Impact of cancer service centralisation on the radical treatment of men with high-risk and locally advanced prostate cancer: A national cross-sectional analysis in England
Matthew G Parry, Arunan Sujenthiran, Thomas E Cowling, Julie Nossiter, Paul Cathcart, Noel W Clarke, Heather Payne, Ajay Aggarwal, and Jan van der Meulen

More than one-quarter of men with high-risk or locally advanced prostate cancer in England do not receive radical treatment with radiotherapy or surgery, potentially owing to differences in treatment access. Here, prostate cancer service centralisation in England was investigated for potential impacts on treatment access. Among English patients in the National Prostate Cancer Audit database, centralisation had no impact on decisions to use radical treatment. It did, however, affect treatment option availability, with potential consequences for patient outcome. Patients were more likely to undergo surgery or high dose-rate brachytherapy when diagnosed at hospitals with direct links to these services.

49 Pre-diagnostic derivatives of reactive oxygen metabolites and the occurrence of lung, colorectal, breast and prostate cancer: An individual participant data meta-analysis of two large population-based studies
Xin Gao, Tom Wilsaard, Eugène HJM Jansen, Bernd Holleczek, Yan Zhang, Yang Xuan, Ankita Anusruti, Hermann Brenner, and Ben Schöttker

Oxidative stress is a well-established cancer risk factor but reactive oxygen species are difficult to measure in patients because of a short half-life. Here the authors focused on serum derivatives of reactive oxygen metabolites (d-ROM), a more stable proxy for reactive oxygen species. By combining data from two large, population-based cohort studies from Germany and Norway, they found that high d-ROM levels were strongly associated with lung, colorectal and breast, but not prostate cancer, findings with potential implications for lifestyle changes in the affected individuals.
Ovarian cancer risk factors by tumor aggressiveness: An analysis from the Ovarian Cancer Cohort Consortium


In ovarian cancer, risk factor profiles may be associated with disease subtypes defined by aggressiveness independent of histology, according to this new analysis. In this large consortium-based prospective study, the authors classified ovarian tumors according to aggressiveness, based on years between diagnosis and death. They hypothesized that pre-diagnosis exposure to risk factors, such as smoking, BMI, family history, and pregnancy, would influence whether an ovarian cancer developed on a path toward more aggressive or less aggressive disease. Indeed, in clustering analysis, risk factor associations tracked by tumor aggressiveness rather than histotypes. Smoking and BMI, two modifiable risk factors, were associated with highly aggressive disease.

The relationship between terminal duct lobular unit features and mammographic density among Chinese breast cancer patients

Hyuna Sung, Changyuan Guo, Erni Li, Jing Li, Ruth M. Pfeiffer, Jennifer L. Guida, Renata Cora, Nan Hu, Joseph Deng, Jonine D. Figueroa, Mark E. Sherman, Gretchen L. Gierach, Ning Lu, and Xiaohong R. Yang

Women with extensively dense breasts carry a heightened cancer risk, a finding well established in the Caucasian population. Here, the authors confirmed this finding in Chinese women by examining the involution of the aging breast, specifically of the terminal duct lobular unit, in relationship to the mammographic density. This extension to an Asian population underscores the model that a higher amount of “at-risk” epithelium due to reduced involution link extensive breast density with breast cancer risk.

Human papillomavirus and p16 in squamous cell carcinoma and intraepithelial neoplasia of the vagina

Hanna Kristina Bertoli, Christina Louise Rasmussen, Freja Lærke Sand, Vanna Albieri, Bodil Norrild, Freija Verdoodt, and Susanne K. Kjaer

Infection with high-risk human papillomavirus (HPV) is suspected of influencing the development of vaginal intraepithelial neoplasia (VaIN) and vaginal squamous cell carcinoma (VaSCC), precursors of vaginal cancer. Here, HPV prevalence and p16 overexpression in VaIN and VaSCC were investigated in a meta-analysis of 26 studies. HPV prevalence was 85 percent and 67 percent in VaIN and VaSCC, respectively, while p16 overexpression was detected in 89 percent of HPV-positive vaginal cancers. The predominant HPV types were HPV16, 33, 18, and 52. The data suggest that HPV vaccination could serve a critical role in VaIN and VaSCC prevention.

Epidemiological, clinical and molecular characterization of Lynch-like syndrome: A population-based study

Noora Porkka, Laura Lahtinen, Maarit Ahtiainen, Jan P. Böhm, Teijo Kuopio, Samuli Eldfors, Jukka-Pekka Mecklin, Toni T. Seppälä, and Päivi Peitomäki

Lynch-like syndrome (LLS), characterized by mismatch repair (MMR)-deficient colorectal tumors that lack MLH1 promoter methylation and germline mutations, remains a diagnostic challenge. Here, LLS was found to account for about 13 percent of MMR-deficient colorectal carcinomas in patients diagnosed in Central Finland between 2000 and 2010. While LLS tumors could not be reliably distinguished from Lynch syndrome (LS) tumors based on clinical or histological factors, LLS tumors differed significantly from sporadic MLH1-methylated and LS tumors DNA methylation and somatic mutation profiles. The findings provide valuable insight into LLS and could facilitate advances in LLS diagnosis and treatment.
Dental fluorosis and oral health in the African Esophageal Cancer Corridor: Findings from the Kenya ESCCAPE case-control study and a pan-African perspective

Diana Menya, Stephen K. Maina, Caroline Kibosia, Nicholas Kigen, Margaret Oduor, Fatma Some, David Chumba, Paul Ayuo, Daniel R.S. Middleton, Odipo Osano, Behnoush Abedi-Ardekani, Joachim Schüz, and Valerie A. McCormack

To date, there are no comprehensive studies of oral health and esophageal cancer in Eastern Africa, nor of this area’s endemic dental fluorosis, an irreversible enamel hypo-mineralization due to early-life excessive fluoride intake. Here, the authors found that moderate/severe fluorosis is associated with a ten-fold increased cancer risk in Eastern Africa, particularly if tooth loss or decay is co-present. The finding is striking because of the remarkable co-location of Africa’s esophageal cancer corridor with areas of high groundwater fluoride. Identification of the causal mechanisms will be critical to primary prevention of this common cancer.

Impact of screening programme using the faecal immunochemical test on stage of colorectal cancer: Results from the IMPATTO study

Massimo Vicentini, Manuel Zorzi, Emanuela Bovo, Pamela Mancuso, Marco Zappa, Gianfranco Manneschi, Lucia Mangone, Paolo Giorgi Rossi, and Colorectal Cancer Screening IMPATTO study working group

Screening programs are intended to reduce mortality by early diagnosis. In this study, the authors evaluated the faecal immunochemical test (FIT) for colorectal cancer. They calculated the effect of FIT screening on stage at diagnosis, and estimated the relative incidence rates by stage. Individuals who attended screening had far higher incidence of stage I cancer, and lower incidence of stage IV, than those not screened. Metastatic cancer incidence, they found, decreased by about 70% at the first round of screening.

Adherence to the Mediterranean diet and lymphoma risk in the European Prospective Investigation into Cancer and Nutrition


Known risk factors explain only a small proportion of lymphoma cases. Several studies have pointed out the potential role of dietary factors on lymphoma risk, but evidence is still inconclusive. Here, using data from the European Prospective Investigation into Cancer and Nutrition study, the authors found for the first time that adherence to a Mediterranean diet was modestly associated with a reduced risk of overall lymphoma. Further studies are needed to confirm these findings.

Evaluation of the transferability of survival calculators for stage II/III colon cancer across healthcare systems

Robert N. Jorissen, Matthew Croxford, Ian T. Jones, Robyn L. Ward, Nicholas J. Hawkins, Peter Gibbs, and Oliver M. Sieber

Survival calculators for colon cancer integrating tumor stage and patient variables are emerging as important tools to assist clinical decision-making. However, so far limited data exist on the transferability of calculators across healthcare systems. The present assessment of five calculators trained on data from either US or clinical trial patients in an Australian community cohort identified deficiencies in calibration for four tools. The findings demonstrate the utility for multi-feature survival calculators to improve overall survival predictions but highlight the need for tailoring of cancer survival calculators prior to adoption across healthcare settings.
Trends in the risk and burden of second primary malignancy among survivors of smoking-related cancers in the United States
Eric Adjei Boakye, Paula Buchanan, Leslie Hinyard, Nosayaba Osazuwa-Peters, Matthew C. Simpson, Mario Schootman, and Jay F. Piccirillo
As more people survive cancer, understanding second primary malignancies (SPMs) is increasingly important. Here, the authors describe the incidence, most common sites, and trends in burden of second cancers in people who had survived one of the top 10 smoking-related cancers. 1 in 12 survivors of smoking-related cancers developed a second primary malignancy, they found. Patients with head and neck cancer had the highest risk of a second cancer, while those with urinary cancers experience the highest excess cancer burden. Oropharyngeal cancers were the most common, and lung cancers represented the largest proportion of the excess burden.

Genetic variants in SLC22A3 contribute to the susceptibility to colorectal cancer
Anjing Ren, Shanwen Sun, Shuwei Li, Tao Chen, Yongqian Shu, Mulong Du, and Lingjun Zhu
The identification of genes or loci associated with colorectal cancer (CRC) susceptibility can facilitate the discovery of molecular pathways underlying CRC development and progression. Here, the authors investigated a risk region at chromosome 6q26-q27, which previously was linked to CRC susceptibility in a Japanese population. Analyses of candidate functional single nucleotide polymorphisms (SNPs) at 6q26-q27 revealed a novel functional SNP, rs420038 G>A, in the SLC22A3 gene. While expression of SLC22A3 was elevated in CRC tissues, the novel SNP was associated with decreased CRC risk in a Chinese population. The A allele of rs420038 significantly suppressed SLC22A3 promoter activity.

The histone chaperone complex FACT promotes proliferative switch of G0 cancer cells
Ling Bi, Chanlu Xie, Mu Yao, Su Su Thae Hnit, Soma Vignarajan, Yilun Wang, Qian Wang, Zhichao Xi, Hongxi Xu, Zhong Li, Paul de Souza, Andrew Tee, Matthew Wong, Tao Liu, Xiaodong Zhao, Jia Zhou, Ling Xu, and Qihan Dong
While solid tumors are known to enter periods of clinical dormancy, how cancer cells reside in this quiescent (G0) state and what circumstances cause them to re-enter the cell cycle to facilitate cancer recurrence and progression remain unanswered. Here, G0 transition to a proliferative state in prostate and lung cancer cells was found to be dependent on the histone chaperone complex facilitates chromatin transcription (FACT). Experiments showed that FACT levels are reduced in G0 cancer cells and restored upon cell cycle re-entry. Re-entry was impeded by FACT silencing, which blocked p27 degradation, an event normally observed when cells resume proliferation.

ETS variant 5 promotes colorectal cancer angiogenesis by targeting platelet-derived growth factor BB
Xi Cheng, Zhijian Jin, Xiaopin Ji, Xiaonan Shen, Haoran Feng, William Morgenlander, Baochi Ou, Haoxuan Wu, Haoji Gao, Feng Ye, Yaqi Zhang, Yi Peng, Juyong Liang, Yimei Jiang, Tao Zhang, Weihua Qiu, Xin Lu, and Ren Zhao
While ETS transcription factors are known regulators of tumor cell invasion, differentiation and angiogenesis, the function of ETS translocation variant 5 (ETV5) remains unknown. In this study, the authors find ETV5 overexpressed in colorectal carcinoma samples and correlate ETV5 overexpression with poor clinical prognosis. They further connect ETV5 to tumor angiogenesis and identify platelet-derived growth factor BB as a direct transcriptional target of ETV5. They propose to target this new signaling axis therapeutically in colorectal cancer.
Loss of KDM6A characterizes a poor prognostic subtype of human pancreatic cancer and potentiates HDAC inhibitor lethality

Shuichi Watanabe, Shu Shimada, Yoshimitsu Akiyama, Yoshiya Ishikawa, Toshiro Ogura, Kosuke Ogawa, Hiroaki Ono, Yusuke Mitsunori, Daisuke Ban, Atsushi Kudo, Shoji Yamaoka, Minoru Tanabe, and Shinji Tanaka

Inactivating mutations in histone lysine demethylase gene KDM6A occur in various tumors, including human pancreatic ductal adenocarcinoma (PDAC). Little is known, however, about the role of KDM6A protein in PDAC. Here, KDM6A knockout in human PDAC cells was found to enhance aggressive characteristics, including mitogenic capacity and invasiveness. KDM6A overexpression downregulated these effects, suggesting a tumor suppressor function for KDM6A. Additionally, H3K27 acetylation levels were downregulated in the promoter regions of tumor suppressor genes including CDKN1A in KDM6A-deficient PDAC, and KDM6A knockout Cells exhibited increased vulnerability to histone deacetylase inhibitors, highlighting the potential of specific therapeutics in PDAC subtypes with poor prognosis.

Synbindin deficiency inhibits colon carcinogenesis by attenuating Wnt cascade and balancing gut microbiome

Luoyan Ai, Yimeng Ren, Yiting Li, Haoyan Chen, Yun Qian, Shiyouan Lu, Antao Xu, Linlin Ren, Shuliang Zhao, Zhaofei Chen, Ying-Xuan Chen, Jie Xu, and Jing-Yuan Fang

The molecular mechanisms that control the development of colorectal cancer (CRC) remain poorly defined. This study reveals that Synbindin, which is a major player in vesicular trafficking, plays a critical role in gut microbiome composition and Wnt signaling activation in colorectal carcinogenesis. Synbindin ablation altered the gut microbiome to a more balanced enterotype and protected mice against tumor formation in the colitis-associated cancer model. In host, Synbindin may act as a novel assembler for DVL3-based signalosome and help to recruit Axin2, orchestrating the intensity of Wnt signaling. Synbindin thus emerges as a potential clinical marker and therapeutic target for CRC.

Non-invasive metastasis prognosis from plasma metabolites in stage II colorectal cancer patients: The DACHS study

Inna Zaimenko, Carsten Jaeger, Hermann Brenner, Jenny Chang-Claude, Michael Hoffmeister, Carsten Grötzinger, Katharina Detjen, Susen Burock, Clemens A. Schmitt, Ulrike Stein, and Jan Lisec

Metastasis is the leading cause of death from colorectal cancer (CRC). New predictive biomarkers are urgently needed, as 25-50% of patients with stage I-III CRC will develop distant metastases after surgery. Here, the authors analyzed plasma from stage-II CRC patients prior to any metastasis, and asked whether plasma metabolites differed between those patients who later developed metastases and those who did not. The answer was 'yes.' The metabolic-profiling models developed in this study were able to correctly predict later metastases in up to 82% of patients.

Microfluidic enrichment, isolation and characterization of disseminated melanoma cells from lymph node samples

Kathrin Weidele, Nataša Stojanović, Giancarlo Feliciello, Aleksandra Markiewicz, Sebastian Scheitler, Barbara Alberter, Philipp Renner, Sebastian Haferkamp, Christoph A. Klein, and Bernhard Polzer

Early metastatic spread to sentinel lymph nodes provides important staging information for melanoma patients. In addition, adjuvant therapies are increasingly explored in node-positive patients, making the availability of companion diagnostics necessary. Thus, here the authors established a protocol for the analysis of single disseminated cancer cells (DCCs) from lymph nodes applying a commercially available epitope-independent microfluidic enrichment method. They show that cell suspension from lymph nodes can be processed and that microfluidics-enriched cells are viable and amenable for subsequent molecular analysis. The presented workflow represents a novel tool for in-depth characterization of lymph node-derived cancer cells, including early metastasis precursors.
242 Profound, durable and MGMT-independent sensitivity of glioblastoma cells to cyclin-dependent kinase inhibition
Emilie Le Rhun, Caroline von Achenbach, Birthe Lohmann, Manuela Silginer, Hannah Schneider, Kristan Meetze, Emese Szabo, and Michael Weller

To date, targeted therapy has remained largely unsuccessful in glioblastoma. The novel brain-penetrating oral multi-kinase inhibitor TG02 has however shown promise as a novel targeted approach and early clinical trials are ongoing. Here, the authors provide a detailed analysis of molecular determinants of sensitivity to TG02 in an extended panel of human glioma models. Human glioma cell lines including glioma-initiating cells were uniformly sensitive to TG02-mediated target inhibition as confirmed by transcriptional suppression of survival genes like mcl-1 and loss of viability. TG02 acted independently of MGMT promotor methylation status, and repetitive exposure to TG02 did not induce acquired resistance.

254 The multikinase inhibitor EC-70124 synergistically increased the antitumor activity of doxorubicin in sarcomas
Oscar Estupiñan, Laura Santos, Aida Rodriguez, Lucia Fernandez-Nevado, Paula Costales, Jhudit Perez-Escuredo, Maria Ana Hermosilla, Patricia Oro, Veronica Rey, Juan Tornin, Eva Allonca, Maria Teresa Fernandez-Garcia, Carlos Alvarez-Fernandez, Alejandro Braña, Aurora Astudillo, Sofia T Menendez, Francisco Moris, and Rene Rodriguez

Wide-spectrum multi-kinase inhibitors may help forestall the onset of drug resistance in cancer. In this paper, the authors tested one such inhibitor, called EC-70124, in sarcoma cells. Sarcoma is typically treated with doxorubicin, but advanced sarcomas often develop resistance by way of ABC transporters, which pump the drug out of the cell. Here, the authors showed that EC-70124 not only slowed tumor growth in vivo, it inhibited the ABC pumps associated with resistance. EC-70124 also worked synergistically with doxorubicin for increased anti-tumor activity.

267 Long-term use of low-dose aspirin for cancer prevention: A 10-year population cohort study in Hong Kong
Kelvin K.F. Tsoi, Jason M.W. Ho, Felix C.H. Chan, and Joseph J.Y. Sung

While long-term use of low-dose aspirin is associated with reductions in the risk of certain cancers, including colorectal cancer, most investigations of aspirin use and cancer prevention have focused on Western populations. Here, the authors examined cancer incidence and aspirin usage in a Chinese cohort. Long-term aspirin use was linked to reduced risk of multiple cancer types, including leukemia and cancers of the liver, stomach, colorectum, pancreas, lung, and esophagus. Reductions were not observed for multiple myeloma or cancers of the kidney, prostate, or bladder, and risk of breast cancer was increased among patients with prolonged aspirin use.

274 Efficacy of anastrozole after tamoxifen in early breast cancer patients with chemotherapy-induced ovarian function failure

In postmenopausal women with hormone receptor-positive breast cancer, aromatase inhibitors (AIs) can prevent disease recurrence and improve survival better than tamoxifen. However, AI-monotherapy should not be used in premenopausal women, as it can stimulate the estradiol production. Here, the authors investigated the effect of the AI anastrozole after prior tamoxifen in women with chemotherapy-induced ovarian function failure (CIOFF) versus postmenopausal women. The Survival was comparable for definitely postmenopausal women and those with CIOFF. However, women with CIOFF whose ovarian function returned had a poorer survival, despite regular monitoring of the estradiol levels.
Efficacy and safety of osimertinib in treating EGFR-mutated advanced NSCLC: A meta-analysis

Lilan Yi, Junsheng Fan, Ruolan Qian, Peng Luo, and Jian Zhang

Epidermal growth factor receptor (EGFR) tyrosine-kinase inhibitors (TKIs) have shown significant promise in treating advanced non-small-cell lung cancer (NSCLC). In this meta-analysis, the authors found that osimertinib, a third-generation EGFR-TKI, is an especially favorable treatment option. Outcomes were encouraging for previously-treated, advanced NSCLCs that carried T790M mutations. In addition, treatment-naïve patients whose advanced NSCLC had EGFR-TKI-sensitizing mutations tended to have a better response with osimertinib than did previous patients treated with earlier-generation EGFR-TKIs. These results indicate that further clinical trials are warranted for optimizing the use of osimertinib in advanced NSCLC.

Concurrent chemoradiotherapy with/without induction chemotherapy in locoregionally advanced nasopharyngeal carcinoma: Long-term results of phase 3 randomized controlled trial


Despite advances in the treatment of nasopharyngeal carcinoma, approximately 30% of high-risk patients experience recurrence after treatment. Here the authors find that combining the conventional chemoradiotherapy with a triple induction chemotherapy (cisplatin/fluorouracil/docetaxel) prolonged survival of patients with locoregionally advanced cancer, even after more than 70 months of follow-up. The combination treatment increased acute, but not late, toxicities, and the authors propose that it could present a new treatment option for this patient group.

The beneficial effect of Mediterranean diet on colorectal cancer

Anna Vittoria Mattioli, Alberto Farinetti, and Roberta Gelmini, MD

Cover Illustration: This figure shows that Synbindin ablation induced a more balanced gut microbiota and decreased Wnt, ERK signaling, which led to less colonocytes proliferation and more enterocytes apoptosis, finally reduced tumor formation. See the related article by Ai et al., pages 206–220.