

Hot Articles

“September|2019”

Health Science



Title: [Apocynin protects retina cells from ultraviolet radiation damage via inducing sirtuin 1](#)
Author: Feng Liu, Chen Lin, Jinsheng Hong, Chuanshu Cai, Weijian Zhang, Jianrong Zhang & Lihong Guo
Journal: Journal of Drug Targeting
Volume: Accepted author version posted online: 03 Sep 2019
Doi: <https://doi.org/10.1080/1061186X.2019.1663527>

Abstract

Direct exposure to Ultraviolet (UV) radiation causes progressive damages in retinal cells, which is one of the hypothetical mechanisms underlying age-related retinopathy or macular degeneration. The protective effects of Apocynin against UV damages were firstly tested in retinal pigment epithelium cells (RPEs) and retinal ganglion cells (RGCs). Subsequently the beneficial effect of Apocynin on mouse retinas against light damage were examined. Next, microarray profiling was used to identify the genes regulated by Apocynin in both RPEs and RGCs. A candidate gene was isolated for functional characterization by knock-down study. Apocynin was shown to inhibit cell death, reduce oxidative stress and deoxyribonucleic acid damages in both RPEs and RGCs challenged with UV. Intravitreal application of Apocynin also improved retinal dysfunction caused by light damage. Sirtuin 1 (SIRT1) was identified as induced by Apocynin by microarray study. The induction was confirmed by realtime-PCR and western blotting. Knocking down SIRT1 antagonized the protective effect of Apocynin against UV damages in both RPEs and RGCs. Apocynin is a novel agent that shows both in vitro and in vivo efficacies against UV radiation induced retina damages. SIRT1 pathway is implicated in UV radiation protection of Apocynin in retinal cells.

Database

Taylor & Francis Online Journals

Title: [Advances in the therapy of BRAFV600E metastatic colorectal cancer](#)

Author: Zhaohui Jin & Frank A. Sinicrope

Journal: Expert Review of Anticancer Therapy

Volume: Published online: 04 Sep 2019

Doi: <https://doi.org/10.1080/14737140.2019.1661778>

Abstract

Introduction: BRAFV600E metastatic colorectal cancer (CRC) is an aggressive tumor subset with an approximate 8% incidence. In these patients, standard chemotherapy has limited efficacy, and the recent development of novel-targeted treatment regimens may significantly improve clinical outcome.

Area covered: This review provides an overview of available data regarding advances in the first-line treatment of BRAFV600E metastatic CRC including patient tumors with microsatellite instability. The implications of BRAFV600E in earlier stage CRC are also discussed.

Expert opinion: Recently, significant progress has been achieved in improving tumor response rates using a novel-targeted regimen in patients with BRAFV600E metastatic CRC. The implications of BRAFV600E in non-metastatic CRC are also becoming more evident and remains an area of ongoing investigation. The majority of CRCs with microsatellite instability high are sporadic and frequently harbor BRAFV600E. All patients with microsatellite instability high metastatic CRCs, irrespective of BRAFV600E, are candidates for immune checkpoint inhibitors. The optimal sequencing of treatment regimens for patients with BRAFV600E metastatic CRCs is an important area for future research.

Database

Taylor & Francis Online Journals

Title: [Radiotherapy in the treatment of primary or recurrent unresectable desmoid tumors of the neck](#)

Author: Xiaoshuang Niu, Rui Jiang & Chaosu Hu

Journal: Cancer Investigation

Volume: Published online: 02 Sep 2019

Doi: <https://doi.org/10.1080/07357907.2019.1656731>

Abstract

Purpose: Desmoid tumors are locally aggressive nonmalignant soft tissue tumors, which frequently recur after therapy. The optimal treatment is still controversial because of the lack of large research. A few studies have reported the effects of other treatments in one lesion when surgery is not possible or would cause notable functional impairment. Our aim was to examine the outcome of radiotherapy (RT) in the treatment of primary or recurrent unresectable desmoid tumors of the neck.

Materials: A retrospective analysis was performed on 30 patients between 1/2008 and 12/2017, with 3 primary and 27 recurrent unresectable desmoid tumors of the neck. All cases were reviewed by pathologists.

Results: The median follow-up time was 50.5 months (range 2–126 months). Radiotherapy doses varied from 50 to 66 Gy (median 60 Gy, 23/30 patients) with all fraction size of 2 Gy. The objective response rate (ORR: CR or PR) to definitive RT was 56.7% (17/30 patients). On Chi-square statistic, ORR was significantly influenced by tumor size (≤ 5 cm versus >5 cm) ($p = .046$). Age (≤ 40 versus >40 years) ($p = .804$), gender ($p = .629$), and RT dose (≤ 60 versus >60 Gy) ($p = .613$) were not significantly associated with ORR. The most common acute side effects of the radiation-related complication were grade 1–2 skin toxicities.

Conclusion: Radiotherapy is a valuable option in the management of primary or recurrent unresectable DTs of the neck with good local control. Multi-institutional and prospective studies are warranted to further validate our findings.

Database

Taylor & Francis Online Journals

Title: [Gender-specific differences in white matter microstructure in healthy adults exposed to mild stress](#)

Author: Sara Poletti, Elisa Melloni, Elena Mazza, Benedetta Vai & Francesco Benedetti

Journal: Stress

Volume: Published online: 03 Sep 2019

Doi: <https://doi.org/10.1080/10253890.2019.1657823>

Abstract

Stress is a powerful moderator of brain plasticity and may affect several physiological functions such as the endocrine and the immune system. The impact of stress can be protective or detrimental according to several factors such as level of the stressor and age of occurrence. Also, the impact may differ in males and females. We aim to analyze the effect of mild levels of early and recent stress on white matter microstructure in healthy volunteers. MRI acquisition of diffusion tensor images with a 3.0 T scanner was performed on 130 healthy subjects (71 males and 59 females). Severity of early and recent stress was rated, respectively, on the Risky Families Questionnaire and on the Schedule of Recent Experiences; subjects were divided into low stress and mild stress groups. Mild early stress associated with lower fractional anisotropy (FA) in the cingulate gyrus compared to low early stress. Females reported reduced FA compared to males in the low-stress group in the internal capsule, posterior corona radiata, posterior thalamic radiation, superior longitudinal fasciculus, and sagittal stratum whereas no difference was observed in the mild stress group. An additive effect of early and recent stress was observed in posterior corona radiata, retrolenticular part of the internal capsule, and superior longitudinal fasciculus. The impact of early stress on WM microstructure in healthy subjects is different in males and females. While males seem to be more sensitive to early stress, an additive effect of early and recent stress manifests itself in females.

Database

Taylor & Francis Online Journals

Title: [Intermediate outcomes of transcatheter pulmonary valve replacement with the Edwards Sapien 3 valve – German experience](#)

Author: Anja Lehner, Tsvetina Dashkalova, Sarah Ulrich, Silvia Fernandez Rodriguez, Guido Mandilaras, Andre Jakob, Robert Dalla-Pozza, Marcus Fischer, Heike Schneider, Gleb Tarusinov, Christoph Kampmann, Michael Hofbeck, Ingo Dähnert, Majed Kanaan & Nikolaus A. Haas

Journal: Expert Review of Medical Devices

Volume: Published online: 30 Aug 2019

Doi: <https://doi.org/10.1080/17434440.2019.1653180>

Abstract

Background: After encouraging results with the Edwards Sapien and XT valves, this study aimed to review procedural data and early outcomes for the Sapien 3 valves for transcatheter pulmonary valve replacement (TPVR).

Methods: We performed a multicenter, retrospective analysis of cases who underwent a Sapien 3 TPVR between 2015 and 2017 in 7 centers in Germany with a follow-up of up to 2 years.

Results: 56 patients could be enrolled (weight $58,5 \pm 25,0$ kg; 53% Tetralogy of Fallot, 45% native RVOT). Most procedures were two-stage procedures (82,1%) with 100% preenting. Valve sizes were 20 mm (n = 1), 23 mm (n = 15), 26 mm (n = 27), 29 mm (n = 13). Procedural success rate was 96.4%. Two patients underwent surgical valve implantation after balloon rupture during TPVR. Follow-up data were available up to 24-month post TPVR. The rate of patients with ? moderate and severe pulmonary regurgitation decreased to 0% after TPVR, peak systolic gradient decreased from 24,2 (SD±20,9) mmHg to 7,1 mmHg (SD±5,0). There were no endocarditis, severe tricuspid valve impairment or stent fractures.

Conclusions: With the Edwards Sapien 3 valve, the patient pool for TPVR can be substantially extended. Continued data collection is necessary to verify long-term results.

Database

Taylor & Francis Online Journals

Title: [A large-scale transcriptome analysis identified ELANE and PRTN3 as novel methylation prognostic signatures for clear cell renal cell carcinoma](#)

Author: Zhongheng Wei, Bo Wu, Li Wang, Juan Zhang

Journal: Journal of Cellular Physiology

Volume: Version of Record online:06 September 2019

Doi: <https://doi.org/10.1002/jcp.29162>

Abstract

DNA methylation was involved in the progress of many types of cancer including clear cell renal cell carcinomas (ccRCCs). This study aimed to identify the prognostic DNA methylation biomarkers for the ccRCCs by a large-scale RNA-seq analysis. The DNA methylation data and the corresponding clinical information of the patients with ccRCCs were extracted from TCGA database and randomly divided into the training group and the validation group. The differentially expressed CpG sites and the survival-related CpG sites were further identified, which was combined into CpG sites pair and followed by screening the survival-related pairs. The C-index and the forward search algorithms were constructed to identify the prognostic signatures for the patients with ccRCCs. The prognostic signatures were verified by the validation dataset and the protein-protein interactions (PPI) network analysis was performed on the CPG sites of the signature. A total of 9,861 differentially expressed CPG sites were identified and 567 CpG sites were found to relate to the overall survival (OS) of the patients with ccRCCs. Besides, 1,146 CPG sites pairs were found to be related to the OS of the ccRCCs samples and the signature composed of seven CpG sites pairs were obtained to predict the prognosis of patients with ccRCCs and the results were verified in the validation dataset. Besides, the PPI network analysis showed that ELANE and PRTN3 gene may be associated with the invasion and metastasis of ccRCCs and could function as potential prognostic and therapeutic signatures for ccRCCs.

Database

Wiley Online Library

Title: [Population Pharmacokinetics of Talazoparib in Patients With Advanced Cancer](#)

Author: Yanke Yu, Chandrasekar Durairaj, Haihong Shi, Diane D. Wang

Journal: The Journal of Clinical Pharmacology

Volume: Version of Record online:06 September 2019

Doi: <https://doi.org/10.1002/jcph.1520>

Abstract

Poly(ADP-ribose) polymerase (PARP) inhibitors have been developed to treat cancers associated with somatic BRCA mutations and germline genetic aberrations involved in the DNA damage response. The efficacy, tolerability, and pharmacokinetic/pharmacodynamic (PK/PD) profile of talazoparib, a potent small-molecule PARP inhibitor, was established in 4 clinical studies in cancer patients (2 phase 1 studies PRP-001 and PRP-002, the phase 2 ABRAZO trial, and the phase 3 EMBRACA trial). The current study aimed to describe the population PK of talazoparib and identify covariates that affect talazoparib PK in patients with advanced cancers using pooled data from these 4 studies. Talazoparib PK was well characterized by a 2-compartment model with first-order absorption and absorption lag time. Based on covariate analysis, no dose adjustment for talazoparib is required based on a patient's age, sex, baseline body weight, Asian race, the presence of mild renal or hepatic impairment, or use of acid-reducing agents. A reduced 0.75-mg daily dose is recommended for patients taking a potent P-glycoprotein inhibitor and those with moderate renal impairment. Insufficient data were available to establish dosing recommendations for patients with severe renal and moderate or severe hepatic impairment. The PK of a single 1-mg talazoparib capsule is comparable with 4 0.25-mg capsules. Talazoparib can be taken with or without food. These data provide support for dosing recommendations and labeling information for talazoparib.

Database

Wiley Online Library

Title: [Development of a high-performance liquid chromatography with tandem mass spectrometry method for identifying common adulterant content in saffron \(*Crocus sativus* L.\)](#)

Author: Weijun Kong, Huijing An, Ji Zhang, Lan Sun, Yao Nan, Aili Song, Lidong Zhou

Journal: Journal of Pharmacy and Pharmacology

Volume: Version of Record online:05 September 2019

Doi: <https://doi.org/10.1111/jphp.13152>

Abstract

Objectives: This study aimed to develop an efficient and reliable method for estimating common adulterants in saffron by detecting their characteristic components to warrant its efficacy and regular use as a highly valuable medicinal herb.

Methods: A selective and sensitive high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) method was developed to estimate the common adulterants in saffron from corn stigma, chrysanthemum and safflower through the simultaneous determination of specific constituents including allantoin, chlorogenic acid (ChA) and hydroxysafflor yellow A (HSYA). Peak identification of each target compound was confirmed from product ions obtained using multiple reaction monitoring triggered enhanced product ions mass chromatogram. Method validation in terms of linearity, sensitivity, reproducibility, accuracy and stability was systematically performed according to official guidelines.

Key findings: Satisfactory separation of the three components was achieved on a C18 column (4.6 × 250 mm, 5 μm) with methanol–acetonitrile–ammonium acetate (3.0 mm) as the mobile phase at gradient elution. The identification of these specific constituents was accomplished using the multiple reaction monitoring mode in combination with enhanced product ion supplementary confirmation. The established method was validated in terms of linearity, sensitivity, reproducibility, accuracy and recovery, which were found satisfactory for sensitive detection of the three target compounds.

Conclusions: By detecting the specific constituents allantoin, ChA and HSYA in one run, the adulterants of corn stigma, chrysanthemum and safflower can be effectively identified and estimated in saffron. This is the first report on developing a simple, sensitive and operational method for the identification and estimation of common adulterants of saffron, that was forwarded for broaden application.

Database

Wiley Online Library

Title: [Internet-based pharmacy and centralised dispensing: an exploratory mixed-methods study of the views of family practice staff](#)

Author: Nicola Hall, Scott Wilkes, John Sherwood

Journal: International Journal of Pharmacy Practice

Volume: Version of Record online:29 August 2019

Doi: <https://doi.org/10.1111/ijpp.12573>

Abstract

Objectives: Over the last decade, technological advances, market competition and increasing pressures for efficiencies across healthcare systems have resulted in changes to the processes and policies involved in medicines prescribing and dispensing. The aim of this study was to explore the views of family practice staff, including GPs, on the perceived impact of changes associated with remote dispensing and the increasing availability of distance-selling pharmacies.

Methods: Exploratory mixed-methods study using qualitative focus groups and an online cross-sectional survey distributed to a non-probability sample of staff from family practices across England. Survey items were developed based on existing literature and initial thematic analysis from the focus groups and adapted using cognitive interviewing techniques.

Key findings: Findings suggest that family practice staff believe that where and how prescriptions are dispensed impacts on their practice and patients. Frequent contact with distance-selling pharmacies is not common; however, highlighted concerns included patient safety issues and the potential threat to the loss of valued elements and sustainability of community pharmacy and dispensing practices. Identified concerns and experiences are unlikely to be routinely discussed within or between practices, limiting opportunities for shared learning and consideration of the potential impact of changes to dispensing processes and policies.

Conclusions: Further research is needed to confirm these exploratory findings, due to the low response rate and sample size. Findings, nevertheless, highlight how wider changes in dispensing processes may have unintended consequences on other aspects of the healthcare system.

Database

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Title: [Positive Oral Contrast Solution at MDCT for Suspected Acute Appendicitis in Adults: Rate of Appendiceal Luminal Filling of Normal and Inflamed Appendixes](#)

Author: Stephen J. Tang, et al. | American Journal of Roentgenology |

Journal: American Journal of Roentgenology

Volume: Ahead of Print, Sep 4, 2019 **Page:** 1-7

Doi: 10.2214/AJR.18.21019

Abstract

OBJECTIVE. The purpose of this study was to assess the rate of appendiceal filling with a positive oral contrast solution at MDCT performed for suspected acute appendicitis in adults.

MATERIALS AND METHODS. We performed a retrospective review of MDCT in 684 consecutive adult patients with suspected acute appendicitis in a 19-month period. Patients were excluded if no positive oral contrast solution (500 mL each of water and polyethylene glycol and 30 mL diatrizoate) was given or if the appendix was not visible or absent. After exclusion, images of 519 patients (mean age \pm SD, 37.4 \pm 16.0 years; 335 women, 184 men) were reviewed for cecal contrast opacification and appendiceal filling. Imaging findings were recorded as positive or negative for acute appendicitis using all available clinical and pathologic data as a reference standard. A control series of CT colonography (CTC) screening examinations (overnight preparation with universal cecal opacification) in 2552 adults without symptoms of appendicitis was also reviewed.

RESULTS. Cecal opacification was confirmed in 313/519 (60.3%) patients, with no difference between those considered to be positive (68/107, 63.6%) or negative (245/412, 59.5%) for appendicitis ($p = 0.506$). When positive oral contrast solution reached the cecum, appendiceal filling was seen in none of the 68 (0%) with appendicitis and in 205 of the 245 (83.7%) without appendicitis ($p < 0.0001$). Among CTC control subjects, appendiceal filling was similar to the cohort considered to be without appendicitis (2240/2552 [87.8%], $p = 0.070$).

CONCLUSION. In MDCT for suspected acute appendicitis, luminal filling of the noninflamed appendix exceeds 80% when positive oral contrast solution reaches the cecum, indicating results similar to screening CTC. The appendix did not fill in proven acute appendicitis, indicating appendiceal filling may allow exclusion of appendicitis with high certainty. These results suggest positive oral contrast solution may augment diagnostic accuracy and confidence in cases of suspected acute appendicitis.

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