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&  
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**PUBLIC HEALTH,  
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# POSTERS

Ales Strancar, Arch Gen Intern Med 2019, Volume 3 | DOI: 10.4066/2591-7951-C2-027

## **NEW TOOLS FOR PURIFICATION AND IN-PROCESS ANALYSIS OF EXOSOMES**

**Ales Strancar**

BIA Separations, Slovenia

Exosomes bring a new set of challenges to purification and equally to in-process analysis. Some of those challenges are in common with proteins, some are in common with virus particles, but many are unique to exosomes. This leads to the conclusion that the traditional tool box needs to be extended. In this poster we introduce a valuable new process tool and two new high through put in-process assay tools. Analytical results from a new approach to exosome purification demonstrate the utility of all three..

### **BIOGRAPHY**

Ales Strancar is the CEO of BIA Separations and one of the main inventors of the CIM Convective Interaction Media® monolithic columns (new generation of chromatographic support). He is author or co-author of more than 90 scientific papers dealing with separation and purification technologies and is now one of top cited Slovenian scientists. He is a co-author of five granted USA patents and their foreign equivalents, more pending, in the field of biomolecule separations and purification. As well he is a co-author of several book chapters dealing with novel chromatography technologies for biomolecule separation. He co-developed a number of industrial scale purification processes among them for Octapharma, Vienna and for Boehringer Ingelheim, Vienna.

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Note:

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## **ASSOCIATION BETWEEN MORTALITY AND HEAT WAVES IN SLOVENIA-LONG TERM ANALYSIS: 2006-2015 VS 1999-2005**

**Simona Perčič<sup>1</sup>, Tanja Cegnar<sup>2</sup>, Katarina Bitenc<sup>1</sup>, Andreja Kukec<sup>3</sup> and Ana Hojs<sup>1</sup>**

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**Background:** Mortality increases during periods of elevated heat in summers.

**Methods:** Author estimated relative risks for mortality for the observed diagnoses, sex, age, and area, as well as 95% confidence intervals and excess deaths associated with heat waves occurring in between 2006-2015 and 1999-2005. For comparison between the two periods, we calculated relative risks ratio and 95% confidence intervals.

**Results:** Statistically significant in 2006-2015 were: age group 75+, all causes of deaths (RR = 1.05, CI 1.01–1.1); age group 75+, all causes of deaths, male (RR = 1.09, CI 1.05–1.14); age group 75+, all causes of deaths, female (RR = 1.09, CI 1.00–1.11); age group 75+, circulatory system diseases (RR = 1.08, CI 1.01–1.16) and age group 75+, all causes of death, urban area (RR = 1.11, CI 1.06–1.17). Statistically significant in 1999-2005 were: age group 75+, circulatory system diseases (RR = 1.11, CI 1.03–1.19) and age group 75+, all causes of death, urban area (RR = 1.14, CI 1.07–1.21). Comparison between 2006-2015 and 1999-2005 revealed no statistically significance between any of the observed subgroups.

**Conclusions:** Slovenian population has not yet adapted to heat waves. Public health efforts are needed and should address circulatory system causes and old age groups.

## **BIOGRAPHY**

Simona Perčič is a medical doctor at National Institute of Public Health in Slovenia. She completed her specialization of Public Health in 2016. Currently her interests are connected with environmental health, concerning especially heat waves, air pollution, water pollution, and other environmental problems. She is a PhD candidate.

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**ACCEPTED ABSTRACTS**

## **DEVELOPMENT OF A SCALABLE PRODUCTION PLATFORM FOR RECOMBINANT ADENO-ASSOCIATED VIRUS VECTORS IN SUSPENSION HEK293 CELLS**

**Lawrence Tam**

Oxford Genetics Ltd., United Kingdom

Recombinant Adeno Associated Viral vectors (rAAV) have emerged as a powerful tool for *in vivo* gene delivery owing to their unique characteristics, including a high safety profile and ability to drive long-term gene expression in humans. Current successes in AAV-mediated clinical trials have prompted pharmaceutical companies to quickly move into the AAV gene therapy market and resulted in growing demand for clinical-grade rAAV vectors. In order to address these requirements, Oxford Genetics has developed a scalable manufacturing platform based on optimized expression plasmids and a clonal cGMP-compliant suspension HEK293 cell line. While this platform facilitates representative material generation for early stage clinical trials, it also allows the transition to packaging and producer cell lines based on the same underlying genetic components, cell line background and process/media system as vector requirements increase. Stable cell lines enable the development of rapid, robust and high-productivity processes, with reduced cost of goods and simplified supply chain. Here we present an update on characterization of these cell lines and internal process development activities to demonstrate associated product quality assurance and scale-up.

## **THE IMPACT OF $\gamma$ -IRRADIATION ON THE INDUCTION OF BYSTANDER KILLING BY GENETICALLY ENGINEERED OVARIAN TUMOR CELLS: IMPLICATIONS FOR CLINICAL USE AS CANCER VACCINES**

**Jehad Zweiri**

University of Liverpool, United Kingdom

Cellular based therapeutic approaches for cancer rely on careful consideration of finding the optimal cell to execute the cellular goal of cancer treatment. Cell lines and primary cell cultures have been used in some studies to compare the *in vitro* and *in vivo* efficacy of autologous vs allogeneic tumour cell vaccines. This study examines the effect of  $\gamma$ -irradiation on a range of tumor cell lines in conjunction with suicide gene therapy of cancer. To determine the efficacy of this modality, a series of *in vitro* and *in vivo* experiments were conducted using genetically modified and unmodified tumor cell lines. Following co-culture of HSV-TK modified tumor cells and unmodified tumor cells both *in vitro* and *in vivo* we observed that the PA-STK ovarian tumor cells were sensitive to  $\gamma$ -irradiation, completely abolishing their ability to induce bystander killing of unmodified tumor cells. In contrast, TK-modified human and mouse mesothelioma cells were found to retain their *in vitro* and *in vivo* bystander killing effect after  $\gamma$ -irradiation. Characterisation of tumor cell death showed that PA-STK cells underwent pyknosis (necrosis) after  $\gamma$ -irradiation. These results suggest that PA-STK cells are not suitable for clinical application of suicide gene therapy of cancer, as lethal  $\gamma$ -irradiation (100Gy) interferes with their bystander killing activity. However, the human mesothelioma cell line CRL-5830-TK retained its bystander killing potential after exposure to similarly lethal  $\gamma$ -irradiation (100Gy). CRL-5830 may therefore be a suitable vehicle for HSV-TK suicide gene therapy. This study highlights the diversity among tumor cell lines and the careful considerations needed to find the optimal tumor cell line for this type of whole cell tumour vaccination.

## **FIELD VALIDATION EXERCISE TO EVALUATE COMMUNITY BASED NAWA JATAN INTERVENTION FOR CHILD NUTRITION**

**Ashish Sinha**

Pt. JNM Medical College, India

Malnutrition is a one of the major social and public health concern in India. Data shows that every 3rd child is underweight in India. There is a similar situation in Chhattisgarh with 37% children underweight. Women and child development department does annual weighing campaign i.e. vajan tyohar, through community participation conducted through growth monitoring and provides community based supplementary nutrition at village level through front-line anganwadi workers. Anthropometric measurement is the main tool to assess the nutrition status of children. An initiative was taken to validate the data reported by front-line workers in Chhattisgarh during the Nawa Jatan ("new care") weighing campaign. A statistically representative sample of children was selected across the state and anthropometric measurement was done by post graduate students of community medicine department. In August 2016 dept. of WCD did a universal weighing campaign for children and 30.13% of them were reported as being underweight. The validation exercise reports 37.76% as being underweight. The underweight children were followed up for next six months with special focus on their supplementary nutrition by front-line workers. After six months of this intervention 41.6% improved their nutrition status and reached normal (out of 30.13% reported underweight in August). As per validation report 39.6% children reached normal (out of 37.76% reported underweight in August). As per WCD department the overall program effectiveness is 41.6% in terms of improving the malnutrition status of underweight children. The validation exercise plays a vital role as supportive supervision and in capacity building of front-line workers. This exercise shows that the problem is bit more than estimated by front-line anganwadi workers. The intervention has improved skills and work outcome of front-line workers.



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## **TOWARDS A 3<sup>rd</sup> GENERATION AAV MANUFACTURING PLATFORM AND IN-PROCESS CONTROLS**

**Ales Strancar**

BIA Separations, Slovenia

**A**deno associated virus (AAV) is the leading vector in the field of gene therapy because of its low toxicity, good overall safety profile and ability to maintain stable expression for long periods of time. It is therefore crucial to develop a robust and high efficiency platform for its manufacturing. One of the key challenges in manufacturing viral vectors is managing the interface between upstream and downstream processing. Experimental observations indicate that, in addition to losses due to shear, processing methods such as precipitation, freeze/thaw and Tangential Flow Filtration (TFF) promote formation of stable associations between virus, DNA and proteins. These complexes lower virus recovery and process capacity, depress robustness, and inflate contamination at each processing step. They accordingly have strong potential to influence long term clinical safety, especially with respect to residual DNA. This paper will present a 2<sup>nd</sup> generation AAV manufacturing platform engineered specifically to address these issues. After removal of cell debris by filtration, AAV is captured and fractionated by hydrophobic interaction chromatography (HIC). The AAV fraction from HIC is diluted and loaded onto a cation exchanger under conditions to dissociate AAV from virus-protein-DNA complexes and strongly bind remaining protein-DNA complexes. The cation exchange fraction is then applied to an anion exchanger as a final DNA dissociation-polishing step and to separate empty and full capsids. This orthogonal process achieves very high recoveries (>70%) with AAVs that are secreted from the host cells. It is fully scalable, very robust, and has proven effective for all AAV serotypes evaluated to date. In addition, the 3-step chromatographic process without preliminary TFF is very efficient and improves overall reduction of all contaminating viruses. A 3<sup>rd</sup> generation process is under development to fully extend these benefits to AAVs processed by cell lysis and to reach extra low DNA impurity profile. Rapid sensitive analytics using multiple in-line HPLC detectors to provide insightful process development and manufacturing documentation will also be presented.



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