International Aspirin Foundation

Senior Science Award Ceremony 2022

Wednesday 28th September 2022

Regent Hotel, Berlin


2022
INTERNATIONAL ASPIRIN FOUNDATION
SCIENCE AWARD
THE INTERNATIONAL ASPIRIN FOUNDATION SCIENCE AWARDS
SENIOR SCIENTIFIC AWARD 2022
AWARDED TO
PROFESSOR
SIR JOHN BURN
FOR EXCELLENCE AND INNOVATION IN CLINICAL SCIENCE
PIPPA HUTCHISON
EXECUTIVE DIRECTOR
SENIOR SCIENTIFIC AWARD 2022
AWARDED TO
PROFESSOR
GIOVANNI DE GAETANO
FOR EXCELLENCE AND INNOVATION IN BASIC SCIENCE
PIPPA HUTCHISON
EXECUTIVE DIRECTOR

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Designed to recognise excellence in different areas of aspirin research, the biennial Senior Science Award is open to individuals and groups with long-term interest and a record of valuable biomedical research that has enhanced the scientific knowledge of aspirin and its impact on human health. In aspirin's 125th anniversary year two awards were made to celebrate ground-breaking work in both basic science and clinical science.

Professor Sir John Burn

received the award for excellence and innovation in clinical science in recognition of his outstanding contribution to defining aspirin's role in cancer prevention, and in particular, the role of aspirin in the prevention of hereditary colorectal cancer (Lynch syndrome) through the CAPP1, CAPP2 and CaPP3 trials – the first of which began in the 1990's and the third of which is ongoing.

Professor Giovanni de Gaetano

has been recognised for excellence and innovation in basic science over 50 years for his work in platelet pharmacology and his seminal contributions to the molecular characterization of the mechanism of action of aspirin on platelet COX-1 that was instrumental to the successful use of low-dose aspirin in the prevention of ischemic cardiovascular disease.

Senior Science Award for excellence and innovation in clinical science

Professor Sir John Burn

Professor Burn expressed a heartfelt thank you on behalf of the whole CAPP team for the Senior Science Award for the research they have carried out investigating aspirin in cancer prevention over the last 30 years.

Professor Burn, a geneticist, became interested in aspirin in the 1980s. He described a family whose teenage son was clearly at very high risk of hereditary bowel cancer as his inspiration to seek out cancer prevention strategies. As a result, in 1993 two approaches were studied in the first CAPP trial, a factorial design looking at daily aspirin and or a high fibre starch or both or neither. Results were mixed but led to the CAPP2 study with its focus on people with Lynch syndrome, a hereditary nonpolyposis colorectal cancer where people with the gene have a 2% per annum risk of cancer in adulthood. CAPP2 included a ten year follow up as it was clear by then that it can take a long time for the aspirin effect to become apparent. A clear effect was seen across all analysis, including the intent to treat analysis, which showed a statistical difference in cancer rates in favour of daily aspirin use. When the incident rate ratio was used on the per protocol analysis [those who took the drug as prescribed] a dramatic 50% reduction in colon cancer was seen for those taking two aspirin a day [600mg] when compared with placebo. Out of 25 people aspirin use prevented one colon cancer over 2 decades – a very successful effect in comparison with many other cancer prevention interventions.

A further analysis of CAPP2 also showed that obese people were more prone to bowel cancer, but this was reduced by aspirin use. This led the researchers to reflect on how inflammation might drive the disease and the role aspirin might play in attenuating this. In nature, salicylates are found in green plants where they have a role in programmed cell death if for example an infected cell is detected. It maybe that people who take aspirin are replacing a similar effect in the body from something we would in the past have obtained from a wild diet. Our more processed diet now is low in salicylates as our plant food is not exposed to infection and therefore not producing salicylates.

With age it has been shown that we lose mitochondrial function in the bowel and are less able to activate the programmed cell death against a cancer cell. This may explain why aspirin is less effective in those over 70 years of age where it is also more prone to cause side effects.

CaPP3 is now underway looking at a twice daily dose of 300 mg aspirin, a once daily 300 mg dose and a 100 mg dose. It is hoped that this study will show a benefit from aspirin with the lower doses as well as in the 600 mg daily dose. CAPP2, with its 600 mg dose, showed no significant difference in important side effects between aspirin and placebo groups indicating that younger people are less sensitive to the gastric issues with aspirin.

Based on the CAPP2 trial result, NICE in the UK now advises doctors to recommend regular aspirin to people with Lynch Syndrome. They identify 150mg and 300mg as possible doses and note that the result of the CaPP3 trial is awaited as a basis for future dosage recommendation. Discussion is underway to consider if other groups at high risk of cancer should also be recommended aspirin cancer prevention therapy. A national team including 'Lynch Champions' are auditing the uptake of the current NICE guideline and encouraging GPs to prescribe aspirin. Professor Burn described his ongoing commitment to this journey with a lot of research still to do and support across his professional Lynch syndrome colleague group for aspirin in cancer prevention.

Senior Science Award for excellence and innovation in basic science

Professor Giovanni de Gaetano

Professor Giovanni de Gaetano, thanked The Foundation for the award and described himself as a medical doctor who has devoted his career to research into cardiovascular disease (CVD) prevention strategies. Professor de Gaetano has been intrigued by aspirin which is formed by a natural polyphenol, salicylate, and a chemical acetyl and how it works to prevent CVD.

Research has shown that by taking aspirin, you are in fact taking two drugs – because aspirin is hydrolysed rapidly into salicylate. When aspirin arrives at the platelets, the salicylate is bound to the binding site and allows the acetyl group of aspirin to acetylate an active site. All the amino acids in this process are now known, but at first they had to just imagine the mechanism by which aspirin worked.

Professor de Gaetano described how they discovered that this mechanism was not only non-specific for salicylate of aspirin but almost all other non-steroidal anti-inflammatory drugs. They demonstrated that indomethacin could bind to the same binding site and prevent aspirin's effect presenting a serious clinical problem. For instance, giving low dose aspirin for preventing cardiovascular events in patients already treated with anti-inflammatories for pain control for rheumatoid diseases is likely to render low-dose aspirin for CVD prevention ineffective. To prevent myocardial infarction, you need to remove all other treatments with non-steroidal anti-inflammatory drugs.

Next, they investigated whether aspirin, an acetylated polyphenol, could interfere with natural polyphenols present in vegetables, fruit, and red wine. They found that these polyphenols could inhibit cyclooxygenase similarly to aspirin but were short acting. Although this could prevent the effect of aspirin the lower concentrations present in red wine potentiated the effect because they act on the same cyclooxygenase receptor but at slightly different points.

This work, understanding variables such as drug and food interactions, translated into a suggestion that in clinical trials the variability of the patients in terms of lifestyle factors need to be considered. The Mediterranean diet is full of polyphenols and perhaps there is a potentiation or perhaps there is a negative interaction, and these factors need to be carefully investigated. Professor de Gaetano advocated for real life clinical trials explaining that randomised clinical trials are so well performed that they don't represent reality and when the general practitioner or cardiologist meets a patient, that patient does not correspond to the patients on whom a randomised clinical trial has shown an effect.

Real world situations need to be investigated, for instance, the socioeconomic condition of people influences the risk of mortality in particular cardiovascular mortality. In addition, consuming ultra-processed food [UPF], food which has undergone strong industrialisation procedures has an effect. Professor de Gaetano and his colleagues have shown in The European Heart Journal recently that people consuming about 20% of their nutritive energy as UPF have a statistically increased mortality risk. Therefore, in a clinical trial the number of people consuming ultra-processed food needs to be considered.

Professor de Gaetano suggested that the way to approach a new generation of randomised clinical trials would be to include less patients but more information on each patient and apply methodologies of artificial intelligence to try to understand the possible interaction between the drug used, in this case aspirin, the lifestyle or other variable, the so-called confounders which can confound the effect of the drug under investigation. In this setting Professor de Gaetano is confident aspirin will show a better efficacy because we will be able to identify patients in whom aspirin is effective and not dilute them in a group of patients who have characteristics not responding to aspirin.

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Making the presentations on behalf of the International Aspirin Foundation, Professor Carlo Patrono, chair of the Scientific Advisory Board said: *"It is a great personal pleasure to recognise the ground-breaking work of Professors Burn and de Gaetano with our 2022 Senior Science Award. Coinciding with aspirin 125th anniversary, the 2022 award feels particularly special because both winners have shown the far-reaching impact of long-term commitment to clinical and basic science in different fields of Medicine, a leit motif of aspirin-inspired research throughout its remarkable life."*

Senior Science Award kindly supported by Bayer AG

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