



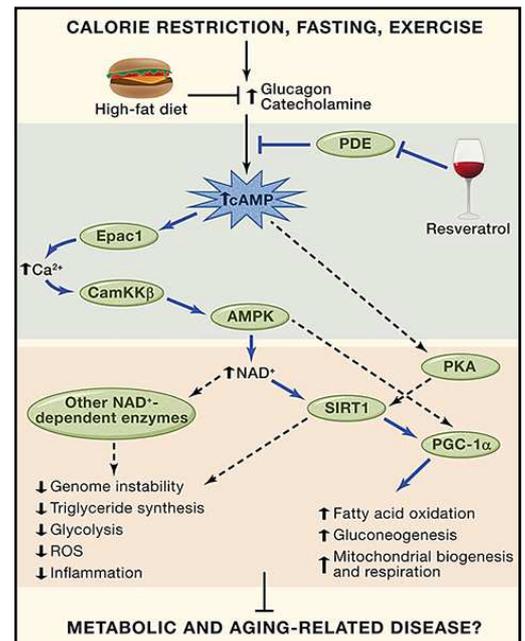
## International Research News

### More light shed on how resveratrol benefits health

Resveratrol is a stilbenoid, a type of natural phenol, found in the skin of red grapes and in other fruits. Red wine contains small amounts of it. Nearly 20 years ago it was proposed that it accounted for the unique effects of red wine on life-span and health. Subsequently, resveratrol was linked to myriad physiological benefits, including protection against cardiovascular disease, cancer, age-related deterioration, and the pathological consequences of high-fat diets. However, the mechanisms whereby resveratrol achieves these benefits is a matter of debate. Some of the researchers who reported resveratrol's beneficial effects founded Sirtris, a biotechnology company, with the goal of battling age-related diseases. In 2008, GlaxoSmithKline paid \$720 million for Sirtris. The company is named after proteins called sirtuins, which have important roles in ageing, and Sirtris' founders contended that resveratrol works, in part, by activating a sirtuin called SIRT1.

However, a number of scientists have since challenged this means of action, arguing that resveratrol does not activate SIRT1 directly, and that the previous results were an artefact of the test used to measure the protein. If this is true, it could complicate efforts to identify and improve drugs intended to work in the same way as resveratrol. In particular, the direct molecular target of resveratrol has been elusive.

Now a new study presents evidence that resveratrol does not directly activate SIRT1. Rather, it found that resveratrol inhibits certain types of proteins known as phosphodiesterases (PDEs), enzymes that help regulate cell energy. The study shows that resveratrol directly inhibits cyclic AMP (cAMP) dependent PDEs, triggering a cascade of events that converge on the important energy-sensing metabolic regulators AMPK, SIRT1, and PGC-1 $\alpha$  (see figure). The authors showed that resveratrol boosts cAMP levels by blocking the PDEs that break cAMP down. When they gave mice a drug that inhibits the PDE that is most abundant in muscle cells, the rodents responded as if they were on resveratrol. They did not gain weight or develop diabetes while on a high-fat diet, and their muscles expressed many of the genes that are triggered by resveratrol. By demonstrating that resveratrol activates the cAMP-Epac1- AMPK- SIRT1 pathway, the study, in conjunction with previous studies, explains how resveratrol activates SIRT1 without directly targeting it. <http://dx.doi.org/10.1016/j.cell.2012.01.017>



### Prions are beneficial in yeast strains

Prions propagate by transmitting a misfolded protein state. When a prion enters a healthy organism, it induces existing, properly folded proteins to convert into the disease-associated prion form; the prion acts as a template to guide the misfolding of more protein into prion form. These newly formed prions can then go on to convert more proteins themselves; this triggers a chain reaction that produces large amounts of the prion. Although often viewed in the context of infectious disease, prions are more loosely defined by their ability to catalytically convert other native state versions of the same protein to an infectious conformational state. It is in this latter sense that they can be viewed as epigenetic agents capable of inducing a phenotypic change without a modification of the genome. Fungal prions are generally nontoxic to their hosts, and a controversial hypothesis that some of the fungal prions, specifically in yeast, are widespread and not associated with any disease state, but may have a useful and beneficial role in some cases, has now been tested.

Some 700 wild yeast strains isolated from diverse environments have been tested for the presence of known and unknown prion elements, finding them in one third of all the strains. All the prions appear capable of creating diverse new traits, with approximately 40% of the traits produced by the wild prions proving to be beneficial to growth in the dozen different environmental conditions tested. These unexpected findings stand as strong evidence against the common argument that prions are merely yeast 'diseases' or rare artefacts of laboratory culture. The study concluded that prions govern heritable traits in nature, in a manner that could profoundly expand adaptive opportunities. <http://dx.doi.org/10.1038/nature10875>

### Mechanisms that influence variability in berry weight and composition reviewed

A review has examined recent ecophysiological, genetic, and molecular knowledge so as to provide better understanding of the mechanisms that influence variability in berry weight and composition. Specifically reviewed was the variation range in berry weight and composition (including sugars, organic acids, and anthocyanins) among *Vitis* genotypes, the environmental and viticulture practices that cause variability for a given cultivar, the genetic clues underlying the genotypic variation, and the

putative genes controlling berry weight and composition (both of which play a role in berry quality and, subsequently, wine typicity). Despite numerous studies comparing differences in the mean value of a berry trait among different environment conditions and viticulture practices, very few studies have explored the level of variation in response to those factors. Present genetic and molecular studies are mainly focused on identifying genes involved in the control of berry weight and composition, with few considerations of environmental factors that affect their expression. The review concluded that, in future, more effort should be directed towards the integration of genetic and molecular work with ecophysiological approaches in an effort to gain novel insights into the cause of variability in grape fresh weight and composition. <http://dx.doi.org/10.5344/ajev.2011.10116>

### Alcohol and heart disease – a new meta-study

A new meta-analysis into the relationship between alcohol consumption and heart disease finds that, while a cardioprotective association between alcohol use and ischemic heart disease (IHD) exists, it cannot be assumed for all drinkers, even at low levels of intake. Based on 44 studies, the analyses used 38 627 IHD events (including deaths) among 957 684 people. There was substantial variation across studies, in particular for an average consumption of one to two drinks a day. The protective association may vary by gender, drinking patterns, and the specific health effects of interest.

Overall the study found that for men the risk function for IHD mortality follows the well-known J-curve with a nadir (lowest point of the curve, i.e., lowest IHD risk) at 31 gms/day. The reversion point, where no statistical evidence for a cardioprotective effect exists, and above which consumption rate there is a positive risk, was reached at 63 gms/day. In women a steeper J-curve was observed, with substantially lower values for the nadir and reversion points (11 gms/day and 14 gms/day, respectively). Binge drinking, even once a month, negated any health benefits obtained from light to moderate drinking. Binge drinking was defined more than four drinks on one occasion for women, and more than five for men.

Moreover, for any particular individual, the review found that the relationship between alcohol consumption and ischemic heart disease should not be isolated from other disease outcomes. Even at low levels, alcohol intake can have a detrimental effect on many other disease outcomes, including on several cancers. The study found support for current low-risk drinking guidelines, especially if these recognized lower drinking limits for women. <http://dx.doi.org/10.1111/j.1360-0443.2012.03780.x>

### Red wine and breast cancer

An increased risk of breast cancer is associated with alcohol consumption, however, it is controversial whether red wine increases this risk. A pilot study of 36 pre-menopausal women observed if there were differences between red wine and white wine in their effects on Aromatase inhibitors (AIs). AIs prevent the conversion of androgens to estrogens, and breast cancers require estrogen to grow. The subjects consumed 237ml of wine daily for two months, either red wine for a month and then white for a month, or vice versa. The investigators concluded that red wine, but not white wine, was associated with significant effects on some indices of estrogen metabolism; free testosterone and luteinizing hormone were increased, but no significant differences were noted in estrogen levels. The data suggest that red wine is a nutritional AI and may explain the observation that red wine does not appear to increase breast cancer risk. <http://dx.doi.org/10.1089/jwh.2011.3001>

## Other News

### DNA sequencing shrinks

By the end of the year a disposable gene sequencing device will go on sale. It is the size of a USB memory stick and plugs into a laptop computer to deliver its results. Expected to cost less than \$900, it will allow small sequencing jobs to be done by researchers who cannot afford to buy a sequencing machine. Called MinION, it is one of the first sequencers to use nanopore sequencing, in which a strand of DNA is read as it is pulled through a microscopic hole. Nanopore sequencing is easy to envision but has been deceptively difficult to carry out.



Minion uses pores made from bacterial proteins. An electric current flows through the pore. The DNA bases interrupt the current in different ways as they go through. One big advantage of the nanopore sequencing is that preparing the sample is quick and easy. No sample amplification is required, and any user-derived sample preparation resulting in double stranded DNA (dsDNA) in solution is compatible with the system. The technology also offers the promise of being able to read tens of thousands of bases in a stretch. Most sequencers read from around 30 to a few thousand bases at a stretch, and these small fragments then have to be pieced together. A possible drawback is the device's error rate. The MinION can be used only once and will sequence up to one billion bases. [www.nanoporetech.com/news/press-releases/view/39](http://www.nanoporetech.com/news/press-releases/view/39)

### Rapid analysis of tannins, phenolics and pigments

The Australian Wine Research Institute has updated its Tannin Portal, which is a web-based application that allows rapid analysis of total tannins, total phenolics, and total pigments in red wines and ferments. No expensive new instrument is required as the method will work with any UV-Vis spectrophotometer. Users simply need to dilute samples in acid, leave them for at least one hour, and then enter six absorbance readings per sample into a web interface which returns results immediately. Users can see the context of their results by benchmarking their data against the AWRI database, selected by region, vintage, age or variety as required. [www.awri.com.au/commercial\\_services/spectral\\_technologies/tannin\\_portal/](http://www.awri.com.au/commercial_services/spectral_technologies/tannin_portal/)

Winetech Scan is available on the Winetech website [www.winetech.co.za](http://www.winetech.co.za)

To subscribe please email Gerard Martin: [marting@winetech.co.za](mailto:marting@winetech.co.za)