SNAPSHOTS

Stress and grey hair
Stress may actually turn hair grey, a study of mice published in *Nature* finds. Harvard scientists saw tha the nerves involved in fight-or-flight reaction are stimulated by stress to affect and permanently damage pigment-regenerating stem cells in hair follicles. During stress, norepinephrine from sympathetic cells causes stem cells to activate excessively.

Warm or cold?
Estimating the temperature of dark matter will give a clue about mass and size of the particles making it up. University of California, Davis, researchers used gravitational lensing to get an estimate. They measured the brightness of seven distant gravitationally lensed quasars to study the effect of intervening clumps of dark matter and estimate their size.

Platypus in peril
A study from Australian University of New South Wales finds that the platypus, a globally unique animal, might be on the brink of extinction. The study estimated that platypus numbers had almost halved because of climate change effects and also land clearing and fragmentation by dams. This has led to the local population extinctions in almost 40% of its range.

A safer alternative to treat aggressive prostate cancer found

Drugs routinely used for treating prostate cancer may actually be worsening the condition

R. PRASAD

A study shows why drugs used for treating prostate cancer which mainly functions by blocking the activity of androgen receptor signalling or stopping the production of androgen or testosterone is actually counterproductive in the long term. While both methods initially produce encouraging results, the cancer very often returns in a more aggressive form, and becomes resistant to these drugs. With cancer no longer responding to these drugs, it grows unchecked and ultimately causes death.

For the first time, the study sheds light into why the FDA-approved drugs against androgen signalling to treat prostate cancer can backfire after initial success.

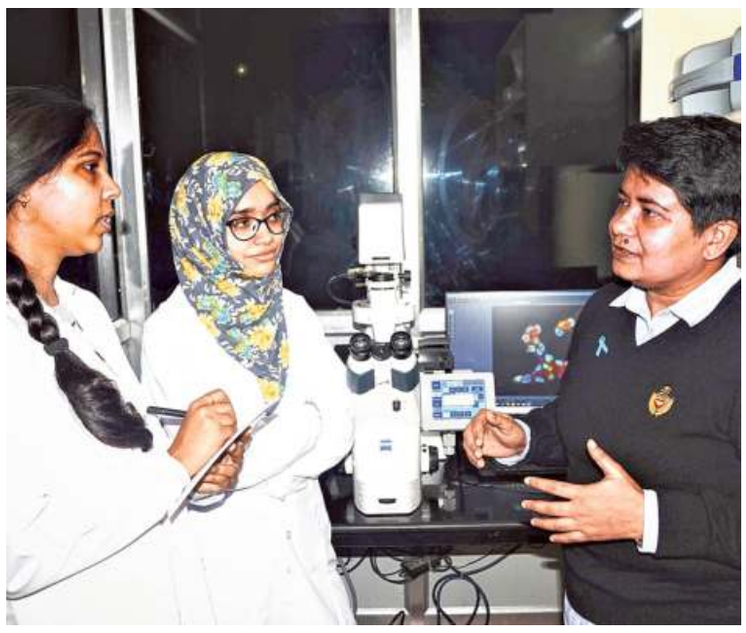
Mechanism of return

The study was done by a multi-institutional team led by Bushra Ateeq from the Department of Biological Sciences and Bioengineering at the Indian Institute of Technology (IIT) Kanpur. The team has also found a mechanism by which the cancer growth at aggressive stage can be safely reduced. The results were published in the journal *Nature Communications*.

Several studies have already shown how stopping the production of androgen or androgen signalling through 'androgen deprivation therapy' at some point unintentionally helps the prostate cancer cells to become resistant towards this therapy and progress further to lethal forms. Now, Prof. Ateeq's team has found the mechanism.

Using mice implanted with prostate cancer tumours, the team found how administering anti-androgen drugs (enzalutamide and apalutamide) results in increase in the expression of a particular gene (SPINK1) which is generally associated with the aggressive type of prostate cancer present in 10-25% of the patients.

"When androgen signalling was inhibited using anti-androgen drugs, an increase in the levels of SPINK1 protein was recorded, which makes the cancer cells more aggressive. The tumours isolated from the mice treated with these drugs exhibit elevated levels of the protein as well as markers for neuroendocrine prostate cancer, which triggers change in cellular plasticity," says Prof. Ateeq.



Counterproductive : The methods currently used produce encouraging results initailly but the cancer often returns in a more aggressive form, say (from right) Bushra Ateeq, Nishat Manzar and Ritika Tiwari.

> **Our study warns about the possible adverse effect of androgen-deprivation therapies, and the benefits must be considered against treatment, before putting the patients on this therapy.**
>
> BUSHRA ATEEQ
> IIT Kanpur

Role of SPINK1 protein

"In another set of experiment, we implanted mice with prostate cancer cells with basal levels of SPINK1 protein and we found manifold increase in the protein levels when we administered anti-androgen drugs," she says. There was also an increase in the levels of neuroendocrine markers which are only found in most aggressive form of prostate cancer. These results reflect a catastrophic situation similar to prostate cancer patients undergoing anti-androgen therapy. Neuroendocrine prostate cancer is an aggressive subtype of prostate cancer which may arise de novo or as a mechanism of resistance due to anti-androgen therapy.

"Our findings emphasise the importance of SPINK1 protein in maintaining neuroendocrine prostate cancer. The results highlight the repercussions of using anti-androgen drugs which are meant to control the prostate cancer but actually aggravate the disease," says Prof. Ateeq.

Repressor of SPINK1

"Using mouse models, prostate cancer cell lines and patients' samples we discovered that androgen receptor functions as a repressor of the SPINK1 gene. Using drugs to inhibit the androgen receptor actually results in stopping the repressive activity of the receptor," says Nishat Manzar from the IIT Kanpur and one of the first authors of the paper. "And this leads to increased level of SPINK1 gene expression."

"We found the SPINK1 gene is also responsible for maintaining the characteristic features of neuroendocrine prostate cancer. The tumour becomes aggressive when the SPINK1 protein level increases while upon inhibiting the protein a decrease in the neuroendocrine markers was observed," says Prof. Ateeq.

In addition to androgen receptor, the researchers found that REST, which is a cofactor of androgen receptor, too, has repressive action on SPINK1 gene. "Our study is the first to show the role of the androgen receptor and REST in repressing the SPINK1 gene expression. This was not known so far," says Prof. Ateeq.

The SPINK1 protein level is high when the amount of REST is low in prostate cancer, and also in the case of neuroendocrine prostate cancer. A particular protein (Casein Kinase 1) is responsible for reducing the level of REST. "When we used an already approved drug to inhibit the activity of Casein Kinase 1 protein, the levels of REST increased," says Manzar.

Clinical trials needed

And when the REST level increases there is a reduction in the SPINK1 protein level accompanied with a reduction in the oncogene properties of prostate cancer cells. Treating prostate cancer cells showing elevated SPINK1 with a drug against Casein Kinase 1 show reduced cancer cell growth as well as aggressiveness.

"We need to conduct clinical trials using Casein Kinase 1 inhibitor to investigate whether it can reverse neuroendocrine prostate cancer and reduce SPINK1 in prostate cancer patients," Prof. Ateeq says.

"Our study warns about the possible adverse effect of androgen-deprivation therapies, and the benefits must be considered against treatment, before putting the patients on this therapy."

Why are there more men than women in the field of STEM?

Masculine culture, insufficient early exposure to science play a role

SPEAKING OF SCIENCE

D. BALASUBRAMANIAN

Across the world, there are more men who are active in science, technology, engineering and medicine (STEM) than women. What is the sociology behind this gender-divide? Research shows that when men and women apply for jobs – be in the labour market, or in places where high level qualifications are demanded, men candidates engage in self-promotion, and are boastful while equally qualified women are more 'modest' and 'undersell' themselves. Even in groups and situations where men and women are present as colleagues, the views of women are either ignored or listened to less seriously than those of men. As a result, women tend to underestimate their ability relative to men, especially in public settings, and negotiate less successfully.

This last point has been particularly brought out in a detailed set of studies by Dr. Sapna Cheryan and colleagues of the University of Washington, Seattle, in their paper: 'why are some STEM fields more gender balanced than others?' (*Psychological Bulletin* 2017;143:1-35, open access). They point out that in the United States while over 60% of BS, MS and PhD degrees in biological and chemical sciences are from women, only 25-30% of them do computer science, physics and engineering. Why this imbalance? The authors suggest three socio-psychological reasons, namely (1) masculine culture, (2) lack of sufficient early exposure to computers, physics and related areas compared to boys in early childhood and (3) gender gap in self-efficacy.

Stereotypes and role models

What is 'masculine culture'? This is due to stereotyping that men are fitter for certain jobs and skills than women, and that women are more 'delicate', 'tender' and thus unfit for 'hard' jobs. In addition, there are not enough female role models whom women may admire and follow. (Of the 866 Nobel winners so far, only 53 have gone to women. And even in life sciences and medicine, of the over 400 Lasker awards, only 33 have gone to women). Regarding point 2, namely, lack of exposure in early childhood to certain fields, the supposed stereotyping of computer field practitioners as 'nerds' with social awkwardness would seem to have played a role from women shying away into other fields.

The third point, namely, the 'gender gap in self-efficacy', appears to have arisen as a result of the above two, and leads to a worry in girls' and women's minds as to 'whether I am really only fit for certain 'soft' fields and jobs (such as in social sciences and life sciences)'– or a feeling of diffidence. This is clearly a reflection and product of masculine culture.

But then, even when we turn to life sciences, where both men and women compete for positions and career advancements in universities and research labs, this gender disparity is glaring. Analysis has revealed that research-intensive universities take fewer women students. It has also been noted that many qualified women scientists have stopped applying for grants from the major national agency, the National Institutes of Health, realising that they may be turned down. An extensive analysis by Lerchenmueller, Olav Sorensen and Anupam B. Jena, titled: "Gender Differences in How Scientists Present the Importance of their Research: Observational Study", has appeared in the 16 December issue this year of *The British Medical Journal* (BMJ 2019;367:l6573, open access; I strongly recommend reading it). Here, they have analysed 1,01,720 clinical research articles, plus 6.2 million papers in life sciences (appearing in PubMed) for the 15-year period 2002 to 2017, and found that women remain underrepresented in the medical faculty and in life science research centres and universities. They also earn lower salaries, receive fewer research grants and fewer citations of their research papers than men colleagues.

India is no better

Men rule the roost here too, and how do they do it? They use more 'buzzwords', boosting their own work than women. A total of 25 such buzzwords are noted by the authors- some of the more frequent ones are: novel, unique, trendsetting, robust, and remarkable. In contrast, women are more modest and thus undersell themselves. Sadly enough, this boasting leads to more grants, leading to faster promotions, salary hikes, plus membership in decision-making committees. This self-perpetuation is a reflection of what Cheryan et al. had described as "machismo". The results of this paper in BMJ were widely reported in the popular press, and one such paper titled it as: 'Male scientists outshout women'!

Are Indian scientists too guilty of this? There surely must be many papers among the 6.2 million that the BMJ paper had looked at where Indian authors figure. We await such an analysis of the grant proposals, decision making bodies and publications in the Indian context. But that such an imbalance exists in India has been made clear by the recent book by Dr. Namrata Gupta, titled: "Women in Science and Technology: Confronting Inequalities" (SAGE Publications India, 2019). She points out that India has been a patrilineal society with the notion that women need not take on jobs, and that this notion has only recently been revised. She points out that women form only 10-15% of STEM researchers and faculty members in the IITs, CSIR, AIIMS and PGIs. In private R & D labs, there are very few women scientists. Alas, we are no better that the rest of the world.

When we turn to research recognition and honours received by Indian scientists, my colleague G. Ponnari points out that the science academies have hardly 10% women, The Bhatnagar Prize has gone to 18 women out of a total of 548 so far, and the Infosys Prize to 15 out of a total of 52. Interestingly, there are no (or a minute percentage of women experts) women in each of these juries.

It would be interesting to study the ratio in research grants offered by the national agencies (such as DST, DBT, SERB, ICMR, DRDO) and do a Lerchenmueller type analysis of grant titles and descriptions (keeping the names and the texts secret so that copyright and propriety rights are not revealed) to check whether Indian men scientists too outshout. May we request the agencies to do so?

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Nilgiris: high pesticide levels in potato, carrot

SHUBASHREE DESIKAN

A study of fruits and vegetables grown in the Nilgiris has found that some of the produce might be harbouring high levels of pesticide, beyond what is considered advisable. This was mainly true of potato and carrot. The study was published in the journal *Food Chemistry*.

While the Food Safety and Standards Authority of India (FSSAI) prescribes a maximum residual level (MRL) for some of the organophosphate pesticides used, it does not prescribe it for some other pesticides used in the cultivation of fruit and vegetables. Hence, the team of researchers took the maximum residual levels from European standards.

Sensitive method

Using liquid chromatography in tandem with mass spectrometry, the team developed a sensitive method to estimate the levels of organophosphates in the fruits and vegetables. "Our detection method has a limit that ranges from 0.1 microgram per kilogram to 1 microgram per kilogram. It has a higher sensitivity than methods used earlier," says S. N. Meyyanathan from Department of Pharmaceutical Analysis, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Udhagamandalam who led the study.

It is known that organophosphate pesticides such as acephate, malathion, profenofos, chlorpyrifos and quinalphos are used in the cultivation of fruits and vegetables. The study measured the levels of these pesticides in 659 samples of fresh fruit and vegetables collected during the agricultural season of 2018-2019. Samples of 18 varieties of fruit and vegetable were collected from four cities of the Nilgiris - Ooty, Gudalur, Kothagiri and Coonoor. Of these, the researchers did not detect pesticides in approximately 57% of the samples. Close to 34% had pesticides used below the MRLs and the remainder – about 8% – showed usage of pesticides above the MRLs.

Potato and carrot

Of the 659 randomly picked fruit and vegetable samples studied, 53 had higher levels of pesticide. These were mainly in strawberry, potato, cabbage, cauliflower, carrot, garlic and broccoli. "About 85% of these samples contained chlorpyrifos, which was the most common, followed by quinalphos at 72%, acephate at 56.6%, profenofos at 54% and malathion at 17%," says S.T. Narenderan who is a PhD student in JSS Academy of Higher Education and Research and the first author of the paper. Among the varieties of vegetables and fruits studied, potato and carrot had the highest usage of these pesticides. "It is essential to control and reduce the level of pesticide. Residual monitoring in fruits and vegetables is important to ensure minimal pesticide residue level to safeguard consumer health," says Narenderan.

Kangaroo mother care improves infant survival

Low-birthweight infants gain from the skin-to-skin contact with their mothers

ASWATHI PACHA

Kangaroo mother care (KMC) or the intervention where babies are placed in skin-to-skin contact with their mothers and exclusively breast fed has been recommended worldwide for stable low-birthweight newborns. Stable babies are defined as babies who do not need respiratory support or intravenous fluids and can accept oral feeds. Though previous studies have shown that keeping the baby in contact with the mother improves survival in babies (less than 2 kg weight at birth) when compared to standard hospital care, global data show that barely 5% receive such care. Also, there is no much evidence on kangaroo mother care impact when initiated at homes in India.

To understand this, a team of researchers led by Nita Bhandari, Director at the Centre for Health Research and Development, Society for Applied Studies, New Delhi, carried out a study in Haryana. The results recently published in *The Lancet* show that kangaroo mother care improved survival by 30% and 25%, in babies till 28 days and six months of age, respectively. The paper adds that such care for all infants with low birthweight could substantially reduce neonatal and infant mortality.

Huge benefit: The care improved survival by 30% and 25% in babies till 28 days and six months of age, respectively.

Developing countries

About 97% of the world's low-weight babies are born in developing countries, and India accounts for about 40% of this, implying an urgent need of effective interventions. Sarmila Mazumder, lead author of the study says, "In developing countries, even today, babies are born at home or even if born in hospitals, are discharged too soon without kangaroo mother care initiation. It is imperative therefore that such care is initiated at home."

For the study, over 8,000 stable low-birthweight babies weighing less than 2.25 kg, were enrolled from two districts in Haryana, during 2015-2018 and randomly assigned to intervention and control groups. Kangaroo mother care intervention was initiated at home, at an average age of 33 hours and delivered during the first month of life, through home visits. The enrolled babies were followed up at one, three and six months of age.

Multiple benefits

Dr. Mazumder adds that kangaroo mother care benefits are much beyond preventing hypothermia. "The care improves exclusive breast feeding, duration of breast feeding, and also reduces infections. It also promotes growth and development of the child and increases mother child bonding, and also reduces stress in both mother and baby," she explains.

When asked how long babies need to be kept in such care, Dr. Mazumder explained that in the study, mothers were advised to keep the babies as long as possible, preferably 24 hours in day and night and till 28 days of age. An average of 11 hours of skin-to-skin contact was achieved, and mothers reported giving kangaroo mother care till 27 days of baby's age. WHO recommends that it be continued till baby attains a weight of 2.5 kg or till babies wriggle out, indicating that they do not need kangaroo mother care any further.

Dr. Mazumder added that an implementation research was also conducted by the same team with the Haryana Government to scale up kangaroo mother care across 16 districts of the state. The paper adds that kangaroo mother care has the potential to prevent thousands of neonatal deaths in our country if 90% coverage can be achieved.

Wuhan: coronavirus cases estimated at 4,000

R. PRASAD

Researchers at the Imperial College London have revised the estimated number of novel coronavirus cases in Wuhan city in China from 1,723 to 4,000. The earlier estimate was made on January 17 and was based on 41 confirmed cases in China as on January 16 and three exported cases - two cases in Thailand and one in Japan. The revised estimate of 4,000 is based on 440 confirmed cases reported from 13 provinces and nine deaths as on January 21, seven exported cases reported from five countries, confirmed human-to-human transmission and confirmed cases in 15 healthcare workers.

Mode of estimation

The estimate has been made by taking into consideration that the Wuhan International Airport has a catchment population of 19 million individuals, a mean 10-day delay between infection and detection, volume of travel from the airport has been 3,301 passengers a day, exit screening that began on January 15 had no impact on exported cases till January 16, and all exported cases are detected at airports outside China.

The researchers note that the estimated cases in Wuhan might be higher than 4,000 if exit screening at Wuhan airport has reduced the number of exported cases and if exported cases are actually more than what has been detected.

"Our estimates of the size of the outbreak in Wuhan have more than doubled since our first report. This is a result of the number of cases detected outside mainland China having increased from 3 to 7," they write.

They caution that the revised estimate should not be interpreted as implying that the outbreak has doubled during the period January 12-18. Rather, the increase in the number of estimated cases only reflect the delay in confirming and reporting exported cases, the small number of exported cases, and incomplete information about dates of symptom onset. These limitations have led to the inability to truly estimate the epidemic growth, they note.