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All eyes on the Nobel Prize

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News

Some people associate the month of September with the end of summer or the start of a new academic year. But September is also the time of year when the process of selecting a winner of the Nobel Prize in Physiology or Medicine begins. It is during this month that the Nobel Assembly, composed of 50 elected members (all professors at the Karolinska Institute in Stockholm, Sweden), sends out nearly 3,000 invitations to nominate potential winners to a select group of individuals. The prizewinner is announced in October of the following year, and although the people involved and the events that transpire during these 13 months are not shrouded in secrecy, most of us are unfamiliar with exactly what goes on during this time. The prize, according to the will of Alfred Nobel, is awarded for a discovery that has changed the scientific paradigm in an important area of life science, explained Goran Hansson, chairman of the Nobel Committee and a professor at Karolinska Institute. “It is important to keep in mind that discovery is the paramount criterion,” Hansson told the JCI. “We make great efforts to identify the initial discoveries and the individuals who made them. Sometimes other scientists may dominate a field when the prize is awarded and those who are not aware of the ‘discovery criterion’ are […]

Trypanosoma brucei, *T. cruzi*, and *Leishmania major*, respectively. Although incidences of these diseases are virtually unheard of in the US, they are endemic in sub-Saharan Africa, Central and South America, Brazil, India, and several other countries. Despite their prevalence, treatment options for these often-lethal diseases are suboptimal and expensive, and vaccines against the parasites have not been developed.

African sleeping sickness, transmitted by the tsetse fly, causes people to sleep for long periods during the day and leads to personality changes and seizures, which become progressively worse. Although 40,000 new cases are reported to the World Health Organization each year, the actual number of cases is probably much higher, since most cases are not reported at all.

Leishmaniasis, transmitted by the sand fly, can cause fever, swollen spleen, severe weight loss, and skin ulcers. The number of new cases of leishmaniasis each year in the world is about 2 million. Triatomine bugs spread Chagas disease, which is characterized by rash, diarrhea, cardiac problems, and enlargement of the esophagus or large bowel. According to the Centers for Disease Control (CDC), an estimated 50,000 of the 16 to 18 million people infected with Chagas disease will die each year.

"Thanks to these studies, scientists are much closer than they were 5 years ago to developing effective drugs against these terrible diseases," said Najib El-Sayed, one of the principal investigators and a lead author on all 3 papers.

The critical finding was that each of the 3 pathogens shared the same 6,200 core genes, which exist in a similar order and represent 70% of the genes present, explained coauthor Peter Myler.

A triatomine bug (left), a vector for Chagas disease; and a sand fly (right), which transmits leishmaniasis. The parasites they transmit have much more in common than was previously thought. Images courtesy of the CDC.

"This is surprising, considering the substantial differences the parasites display," El-Sayed told the *JCI*. Each organism is transmitted by a different insect, infects a different set of tissues, has unique life cycle features, and causes very different symptoms and diseases.

"They also employ different immune evasion strategies," El-Sayed explained. "*L. major* hides within the very same cells of the immune response and alters the function of the macrophages it infects, *T. cruzi* expresses a complex variety of surface antigens from within the cells it infects, while *T. brucei* remains extracellular but circumvents the host immune response by the periodic switching of its major surface protein."

Nevertheless, the gene order and organization — called the synteny — along the parasite chromosomes is conserved. "This suggests that whole batches of genes are transcribed together and that regulating the activity of genes is very simple," Berriman said. "If we can find an exploitable weakness amongst those common genes, we may be able to devise an intervention strategy that works on all 3 parasites."

The genetic similarities uncovered among the parasites prevail over the differences, providing scientists with the opportunity to develop drugs to target all 3. On the other hand, detailed analysis of their variations could lead to targeted therapy against each parasite in particular.

A long-term goal for El-Sayed is to revitalize efforts to develop drugs against these neglected diseases. He is also sequencing the genome of *Schistosoma mansoni*, the causative agent of schistosomiasis, a disease caused by parasitic worms affecting 200 million worldwide.

"Genome sequences do not in themselves cure people," El-Sayed said. "However, they do bring the prospect of safe and effective drugs, vaccines, and diagnostics nearer to fruition."

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Linda B. Buck leaves the podium after receiving the Nobel Prize in Physiology or Medicine for her work on olfactory receptors from Swedish King Carl XVI Gustaf at the December 10, 2004, ceremony at the Concert Hall in Stockholm. Photo credit Sven Nackstrand/AFP/Getty Images.

the initial discoveries and the individuals who made them. Sometimes other scientists may dominate a field when the prize is awarded and those who are not aware of the 'discovery criterion' are surprised when the Nobel Prize goes to the initial discoverer rather than to those who are seen as leaders later on."

The privileged few who may submit proposals for nominees of the Nobel Prize in Physiology or Medicine are chosen on the recommendation of the Nobel Committee, the 6-member working body of the larger Nobel Assembly.

Among those selected to make nominations are members of the Nobel Assembly and Nobel Committee at the Karolinska Institute; members of the medical class of the Royal Swedish Academy of Sciences; Physiology or Medicine Nobel laureates; established professors at the faculties of medicine in Sweden, Denmark, Finland, Iceland, and Norway; established professors at no fewer than 6 other medical institutes selected by the assembly; and other scientists whom the assembly deems worthy of this opportunity.

Once this list is amassed, the Nobel Assembly sends out invitations, which are due back by February. In a typical year, 200 to 300 candidates are nominated. The members of the Nobel Committee sort through the nominees with the help of 10 expert advisers.

"We go through the hundreds of nominations, make brief written evaluations on every nominated candidate, and identify those candidates that need a more in-depth evaluation," said Hansson. "Experts in house and around the world are asked to provide detailed, scholarly, and secret reports on the top candidates. These reports serve as a basis for the final part of the decision process, which takes place in September." At this time, nearly one year later, the committee presents its choices to the Nobel Assembly.

Hansson told the *JCI* that a candidate or research field is often analyzed repeatedly over several years before a final decision is made. While some Nobel laureates are awarded the prize the first time they are nominated, many others are nominated several times before winning. Robert Koch was nominated 55 times before he received the prize in 1905 for his investigations of tuberculosis. Ferdinand Sauerbruch was not so lucky, being denied the prize despite 54 nominations over 14 years.

On the first Monday in October, the Nobel Assembly votes on 1, 2, or 3 candidates for that year's prize, and their decision is final. The secretary of the Nobel Assembly calls the winners immediately afterward, and a press conference is held later that day.

The physical prizes — a medal, a personal diploma, and a financial award — are presented on December 10, the anniversary of Nobel's death. The new winners are invited to lecture in the Stockholm Concert Hall and partake of celebrations along with the king of Sweden and the royal family. By this time, a new round of potential Nobel Prize winners are being considered for the following year.

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Nobel blunders

The international scientific community tends to agree with most of the decisions made by the Nobel Assembly, and the Nobel Prize remains the most prestigious award in science, but it is not without a certain degree of controversy.

The main criticisms surrounding the Nobel Prize awards are that the foundation has overlooked deserving people, mistakenly given the award to someone other than the initial discoverer or whose work did not prove worthy, and failing to recognize women. The leading example of an omission was Oswald T. Avery, who discovered in 1944 that DNA carried genetic material. Although Avery was nominated many times, his data were met with skepticism from the scientific community, which at that time believed that proteins carried genetic material. By the time his ideas were accepted, Avery had passed away.

Three leading cases of a mistake being made regard Nobel Prizes awarded to Frederick Banting and John Macleod in 1923 for their discovery of insulin, which was actually made by Banting and Charles Best in Macleod's laboratory while Macleod was away; to Johannes A.G. Febiger in 1926 for his discovery of *Spiroptera carcinoma*, an agent that supposedly induced cancer in mice, but could never be replicated and was later discredited; and to Egas Moniz in 1949 for use of lobotomy to treat psychiatric patients, which today is considered unethical.

A mere 6 of the Nobel Prizes awarded in Physiology or Medicine have gone to women. But this is not surprising, since men outnumbered women in the biomedical sciences during the 1900s. The first woman to win a Nobel Prize was Marie Curie in 1903, only 2 years after the Nobel Foundation was established.