



Research brief

Tip for a new vaccine

An experimental therapeutic human papillomavirus vaccine called Tipapkinogen Sovacivec (Transgene; Illkirch, France), seems to be able to clear infection in about a third of women with high-grade lesions. It is a targeted immunotherapy vaccine that includes a specific protein to trigger immune responses to high-risk human papillomavirus types. Researchers enrolled nearly 200 women with cervical intraepithelial neoplasia (CIN) grade 2 or 3 lesions, giving them either the treatment or placebo (2:1) followed by standard surgery 6 months later. Women who received the treatment were twice as likely as those given placebo to have their CIN eliminated. 21% of women with highest-risk CIN3 lesions who received treatment had complete resolution of their CIN3, versus no women given placebo. The therapy could also work in other types of cancers, such as head and neck cancer and anal cancer.

HIV: gut composition a good indication

The gut microbiomes of men who have sex with men (MSM) differ in composition from those of men who have sex with women (MSW), irrespective of HIV infection status. To assess whether these differences affect the risk of HIV transmission, researchers transplanted stool samples from HIV-negative MSW and MSM and HIV-positive MSM into germ-free mice. The signature microbiotic compositions of MSM successfully engrafted into mice and were associated with increased activation of CD4 and CD8 cells in the mice. Experimental HIV infection of human cells showed higher infection rates in cells exposed to isolated fecal microbiota of MSM compared with MSW. These findings suggest that an individual's gut microbiota could be a risk factor for HIV transmission.

Out of cyt

Owl monkey cytomegalovirus evades the immune system by producing molecules to thwart immunological attack. They make homologues for CD48, a ligand of the 2B4 receptor on immune cells such as natural killer cells. In a study of animal cells, researchers showed how A43, one such CD48 homologue, binds to 2B4 with high affinity and slow dissociation rates. The soluble A43 can effectively block interaction between CD48 and 2B4 and can thus suppress the body's cytotoxic lymphocyte response. These findings show a new way in which viruses evade the mammalian immune system. Further study of A43 could lead to treatments for autoimmune diseases.

Making Zika weaker

The potential of traditional monoclonal antibody treatments is restricted by the need for high doses, long diffusion times, and a cold chain. To side-step these problems to develop a therapy for Zika virus, researchers have developed DMAB-ZK190, a synthetic monoclonal antibody fully encoded on cDNA sequences that instructs the body's own cells to produce the antibody themselves. Eight mice injected with the vaccine survived an otherwise lethal dose of the virus, with no symptoms. Three injections of DMAB-ZK190 controlled infection in five rhesus macaques, lowering viral load in four.

Shedding light on MRSA

Researchers in the USA have discovered that exposing otherwise stubborn methicillin-resistant *Staphylococcus aureus* (MRSA) to specific wavelengths of blue light can render it susceptible to bactericidal agents, such as hydrogen peroxide. They showed that low-level 460 nm light can photolyse staphyloxanthin, an antioxidant in the bacterium's membrane, leaving it vulnerable to hydrogen peroxide in a series of experiments in culture,

in infected macrophages, in biofilms, and in two mouse models of wound infection. The researchers hope that in only a few years' time a small light-emitting wound-healing device could be available.

New treatment unleashed

GSK3494245/DDD01305143/compound 8 is a small molecule with a big name and big potential to work as an oral treatment for visceral leishmaniasis (caused by *Leishmania donovani* and *Leishmania infantum*). Most of the current treatments for the disease are unsuitable for wide-scale use because they are highly toxic to people, have problems with resistance, or require patients to be admitted to hospital for treatment. Researchers discovered the new compound when trawling through findings from a previous screen against the related parasite *Trypanosoma cruzi*, which causes Chagas disease. In initial laboratory experiments, the compound showed a promising pharmacokinetic profile and in vivo efficacy against *L donovani* in a mouse model (>95% reduction in parasite load).

One of a kinetoplastid

Findings from a study of *Trypanosoma brucei*, the parasite that causes sleeping sickness, suggest that the way in which it regulates an essential cellular signalling pathway differs from that of all other eukaryotes. Scientists synthesised an activator that bound to the essential protein kinase A (PKA). cAMP, which binds PKA in every other known nucleated cell, does not bind PKA in the parasite. Further understanding of the differing mechanisms could lead to a treatment that inhibits trypanosome PKA, but leaves the mammalian host unaffected. The finding could be applicable to other diseases caused by kinetoplastid parasites, such as Chagas disease and leishmaniasis.

Dara Mohammadi

For more on **therapeutic human papillomavirus vaccination** see *Gynecol Oncol* 2019; published online April 4. <https://doi.org/10.1016/j.ygyno.2019.03.250>

For more on the **microbiome and HIV** see *PLoS Pathog* 2019; **15**: e1007611. <https://doi.org/10.1371/journal.ppat.1007611>.

For more on **cytomegaloviruses and immunity** see *PLoS Pathog* 2019; **15**: e1007658. <https://doi.org/10.1371/journal.ppat.1007658>

For more on **Zika virus vaccination** see *Mol Ther* 2019; published online April 5. <https://doi.org/10.1016/j.ymthe.2019.03.005>

For more on **light and MRSA** see *Advance Sci* 2019; published online March 30. <https://doi.org/10.1002/advsc.201900030>

For more on a **potential treatment for leishmaniasis** see *Proc Natl Acad Sci USA* 2019; published online April 8. <https://doi.org/10.1073/pnas.1820175116>.

For more on **Trypanosoma signalling** see *Nat Commun* 2019; **10**: 1421. <https://doi.org/10.1038/s41467-019-09338-z>.