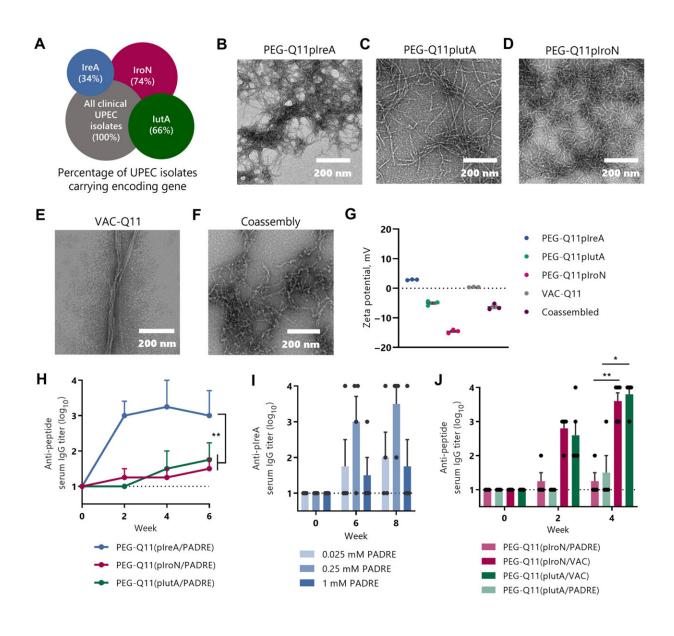


A possible vaccine against the bacteria that cause UTIs

November 25 2022, by Bob Yirka



Sublingual nanofiber vaccine raises antibody responses against three B cell epitopes with broad expression across UPEC strains.(A) Percentage of clinical



UPEC isolates that contain the gene encoding the parent proteins of the pIroN, plutA, and plreA epitopes (2). Transmission electron microscopy images of nanofibers composed of (B) PEG-Q11pIreA, (C) PEG-Q11pIutA, (D) PEG-Q11pIroN, and (E) VAC-Q11, or (F) a coassembly of these four together. (G) Zeta potential measurements of nanofiber assemblies. (H) Mice were immunized sublingually with coassembled PEG-Q11 nanofibers containing the PADRE T helper epitope and either pIreA, pIroN, or pIutA B cell epitope, plus cholera toxin B (CTB) adjuvant. Mice were boosted at weeks 1 and 3, and serum immunoglobulin G (IgG) titer against the immunizing epitope was measured [two-way repeated-measures analysis of variance (RM-ANOVA), Tukey's test, n = 4 per group]. (I) Effects of titrating T cell epitope content with sublingual nanofiber vaccines. Mice were immunized sublingually with PEG-Q11(pIreA/PADRE) nanofibers containing variable concentrations of PADRE plus CTB and were boosted at weeks 1, 3, and 6 (n = 4 per group). (J) Coassembly with the VAC epitope, but not PADRE, elicits antibody responses against plutA and plroN. Mice immunized with the plutA or plroN epitope and VAC are compared to responses with PADRE shown in (F). All mice were boosted at weeks 1 and 3, and formulations contained CTB adjuvant (two-way RM-ANOVA, Tukey's test, n = 4 per group). Credit: Science Advances (2022). DOI: 10.1126/sciadv.abq4120

A team of researchers at Duke University has developed a vaccine against uropathogenic E. coli (UPEC), the type of bacteria that cause urinary tract infections (UTIs) in humans. In their paper published in the journal *Science Advances*, the group describes how they made their vaccine and its performance when tested in mice and rabbits.

Urinary tract infections are most common in women and can produce extreme pain during urination—they can also lead to other complications that, if not treated, can be fatal. Such infections are generally treated with antibiotics. Unfortunately, some women develop chronic infections, which means they experience UTIs several times a year.



In such circumstances, it becomes problematic to continue to prescribe antibiotics because they kill all the bacteria in the gut, which tends to cause other intestinal problems. In this new effort, the researchers have taken a new approach to dealing with UTIs, avoiding antibiotics in general and instead creating a pill that targets only the bacteria behind the infection.

Scientists have been trying for many years to create a vaccine for UTIs, but have failed, mainly due to problems with getting a medication to penetrate the cellular mucosa that coats the walls of the mouth, throat and <u>urinary tract</u>. To overcome this problem, the researchers tried a variety of approaches that involved manipulating drugs that were able to penetrate cellular mucosa.

They developed a kind of peptide nanofiber that could not only penetrate the mucosa, but could train the <u>immune system</u> to recognize and fight UPEC by exposing it to three peptides that reside on the surface of the bacteria. The vaccine delivery method was found to elicit an <u>immune response</u> in the urinary tract due to similarities between the <u>mucous membranes</u> lining the urinary tract and the mouth. The pills the team created were administered under the tongue and are dissolved in saliva.

In testing their vaccine in mice and rabbits, the researchers found it to be as effective as traditional antibiotics and determined that its repeated use did not lead to gastrointestinal problems. If the <u>vaccine</u> proves to be effective in humans, it would greatly reduce the number of antibiotics used to treat diseases overall, slowing the progression of bacterial resistance to available antibiotics.

More information: Sean H. Kelly et al, A sublingual nanofiber vaccine to prevent urinary tract infections, *Science Advances* (2022). DOI: 10.1126/sciadv.abq4120



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Citation: A possible vaccine against the bacteria that cause UTIs (2022, November 25) retrieved 4 February 2023 from https://medicalxpress.com/news/2022-11-vaccine-bacteria-utis.html

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