Genome sequence of a vancomycin resistant pathogen

*Enterococcus faecalis* is an important opportunistic pathogen that is among the leading causes of a range of infections in the USA, including urinary tract infections, bacteraemia and infective endocarditis. The resistance of *E. faecalis* to a broad range of antibiotics including vancomycin has lead to the emergence of *E. faecalis* as an important nosocomial pathogen that is refractory to most therapeutic options. The 3.3 megabase genome sequence of a vancomycin resistant isolate sequence of *E. faecalis* was determined. More than a quarter of the genome consisted of mobile elements: DNA that can move around on chromosomes, among organisms and between species. This is one of the highest percentages of mobile elements described for a bacterium, and these mobile elements carry vancomycin and drug resistance genes as well as known and putative virulence genes. The preponderance of mobile elements probably contributed to the rapid acquisition and dissemination of drug resistance in the enterococci and emphasizes their potential for passing resistance and virulence genes between strains and species. Recent reported incidents of the emergence of vancomycin resistant *Staphylococcus aureus* clinical isolates from transfer of enterococcal genes provides a concrete example of this threat.

I.T. Paulsen
The Institute for Genomic Research,
9712 Medical Center Drive, Rockville, MD 20850, USA
E-mail address: ipaulsen@tigr.org (I.T. Paulsen).

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Postmenopausal hormone therapy and coronary artery atherosclerosis

In randomized controlled trials of postmenopausal women with established coronary artery disease, conjugated equine estrogen with or without daily continuous combined medroxyprogesterone acetate has failed to reduce atherosclerosis progression. Many questions remain as to the effectiveness of other estrogenic compounds, dosages, regimens and routes of administration. Whether 17β-estradiol (the bioidentical molecule) alone, or given sequentially with medroxyprogesterone acetate can reduce atherosclerosis progression is uncertain.

The Women’s Estrogen–Progestin Lipid-Lowering Hormone Atherosclerosis Regression Trial (WELL-HART) was a randomized, double-blind, placebo-controlled serial arterial imaging trial designed to test the effects of oral micronized 17β-estradiol with or without sequentially administered medroxyprogesterone acetate on the progression of atherosclerosis in postmenopausal women with coronary artery disease. WELL-HART was comprised of 226 women (average age = 63.5 years) who were on average 18 years postmenopausal with at least one coronary artery lesion ≥30% diameter stenosis. In addition to the randomized treatment of hormone therapy vs. placebo, LDL-cholesterol was reduced to a target goal <130 mg/dl (3.36 mmol/l) with dietary intervention and lipid-lowering therapy. The primary trial outcome was the average per-participant change in lesion percent diameter stenosis by quantitative coronary angiography. After an average of 3.3 years of intervention, the mean (S.E.M) progression in percent diameter stenosis (%) was 1.89(0.78)%S, 2.18(0.76)%S and 1.24(0.80)%S in the usual care, unopposed 17β-estradiol and sequential medroxyprogesterone acetate + 17β-estradiol treatment groups, respectively (P = 0.66). The mean (95% confidence interval) difference in progression between 17β-estradiol and sequential medroxyprogesterone acetate + 17β-estradiol vs. usual care was 0.29%S (–1.88%S–2.46%S) and –0.65%S (–2.87%S–1.57%S), respectively.

WELL-HART demonstrated that 17β-estradiol unopposed or sequentially opposed with medroxyprogesterone acetate had no significant effect on the progression of atherosclerosis in elderly postmenopausal women with established coronary artery atherosclerosis who were on average 18 years postmenopausal. WELL-HART stands in contrast to the beneficial effect of unopposed 17β-estradiol on the progression of subclinical atherosclerosis in postmenopausal women without preexisting cardiovascular disease who were on average 13 years postmenopausal in the Estrogen in the Prevention of Atherosclerosis Trial (EPAT), a sister study to WELL-HART. These two contrasting trials indicate that estrogen therapy may be effective in reducing the progression of atherosclerosis when initiated early in menopause while the vascular wall remains responsive to estrogen. Several lines of evidence now support this hypothesis. The difference