



## Study Suggests High TB Rate in Inuit Populations Not Due to Enhanced Virulence

Oct 20, 2015 | [Andrea Anderson](#)

NEW YORK (GenomeWeb) – Higher-than-usual tuberculosis rates in Inuit populations in Nunavik, Quebec do not appear to stem from enhanced virulence features in the *Mycobacterium tuberculosis* genome, according to a new [study](#) in the *Proceedings of the National Academy of Sciences*.

"[O]ur findings suggest that *M. tuberculosis* has not thrived in Nunavik due to a unique virulence profile of the bacteria," authors of the study noted. "It follows that *M. tuberculosis* control in this region, and in similar settings, will require looking beyond the bacterial culprit to the social conditions that foster TB."

Researchers from McGill University and elsewhere sequenced and compared the genomes of more than 150 of the clinical *M. tuberculosis* isolates collected in Nunavik between 1990 and 2013. Using two different dating methods, they estimated that *M. tuberculosis* arrived in the region in around 1919 or 1920.

"Whether you were in the same village or you were in a different village, all the bacteria seemed to have a relatively recent ancestor," corresponding author Marcel Behr, a tuberculosis researcher with the McGill University Health Centre, told GenomeWeb.

The team's genetic data suggests that *M. tuberculosis* has been subject to weak selective pressure and genetic drift since arriving in the region. But it did not see signs of increased pathogen virulence.

During an epidemic TB event that infected dozens of people from a 933-person village in Nunavik in 2011 and 2012, Behr and his team found that the genetic diversity was so low in the culprit *M. tuberculosis* strain that they needed to use whole-genome sequencing to tease apart bacterial transmission patterns — work they [described](#) early this year in *The Journal of Infectious Diseases*.

"Because there was limited bacterial diversity in the strain we were studying, we needed to do whole-genome sequencing to be able to finally resolve the transmission networks in 2012 in one village," Behr said. "Having noted that almost all of the bacteria in that village seemed to have descended from a single ancestor ... we decided to expand across the 14 villages of Nunavik."

The Nunavik region experienced an uptick in TB cases in the 1940s and 1950s, he explained. The disease waned in the 1980s and 1990s, but resurged again over the past decade or more.

Currently, the rate of TB infection amongst Nunavik's Inuit populations is roughly 50 times higher than that observed in most other parts of Canada.

To investigate potential sources for such TB epidemics and the potential role of enhanced bacterial virulence in this process, Behr and his colleague focused on 149 isolates collected from across 14 Inuit communities in the Nunavik region from 2001 and 2013, along with 26 more isolates collected in the area between 1990 and 2000.

Using Illumina's MiSeq instrument, the team successfully sequenced 163 of the isolates to average depths of almost 45-fold coverage across the 4.4 million base *M. tuberculosis* genome.

Pairwise analyses of the Nunavik isolates again supported the notion that *M. tuberculosis* diversity is low in the region: isolates from the same village typically differed at a handful of bases or less, while strains from different villages had between 40 and 60 distinct base pairs, on average.

As a group, the isolates were prone to non-synonymous SNP substitution patterns reflecting weak positive selective pressure on the pathogen and high rates of transmission, the team reported. It also saw signs of genetic drift in the pathogen, including the introduction of deletions altering genes that were previously deemed essential for *M. tuberculosis* growth.

When they compared these sequences to one another and to the genomes of *M. tuberculosis* from three representatives apiece from the seven main TB lineages, the researchers found that all of the Nunavik isolates fell into a European-American TB lineage known as lineage 4.

Using *M. tuberculosis* mutation rates documented in past studies of the bug, combined with their data from the northern Quebec communities, the researchers estimated that isolates in the area are descended from a common ancestor introduced to Nunavik in around 1919.

A parallel analysis based on mutation rates detected in the isolates themselves over the 23 years they were collected led the team to a similar conclusion, again placing the introduction in the early 20<sup>th</sup> century.

"There seems to have been a single-source introduction by one person who brought in one bacterium," Behr said. "One hundred and fifty three genomes, a century later, are all descended from that introduction."

It is unclear whether this ancestral isolate made its way to the region via an infected individual from Europe, other parts of North America, or elsewhere, he explained.

Still, since the form of *M. tuberculosis* circulating in the region appears to be drug susceptible and no more virulent than usual, Behr noted that public health efforts and the availability of rapid diagnostic methods will likely be need to find, treat, and curb the spread of TB in the region.

He and his colleagues are continuing to explore the factors and *M. tuberculosis* features that may contribute to TB outbreaks in Nunavik and elsewhere.

"We continue to have tuberculosis in the north," Behr said, "and we have to try to better understand why so that we can intervene."

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