

Mid-Study Report to PHI

Summary of Poliovirus Genome in Patients with Post-Polio Syndrome

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In late 2013, Post-Polio Health International awarded \$100,000 to the team of Antonio Toniolo, MD; Andreina Baj, MD; Martina Colombo, PhD – Laboratory of Medical Microbiology and Virology, Department of Biotechnology and Life Sciences, University of Insubria Medical Center, Varese, Italy, to expand its search for poliovirus genome in various populations. The team’s work is enhanced by the expertise of Konstantin

Chumakov, PhD, Associate Director for Research, Office of Vaccines Research and Review, FDA Center for Biologics Evaluation and Research, Silver Spring, Maryland.

The goals are: 1) to complete the systematic search of poliovirus genomes in the Italian cohort of post-polio syndrome cases, and 2) to verify if poliovirus genomes are also present in aging polio survivors with “stable polio” (i.e., those aged >60 years that have not developed post-polio syndrome).

The team will compare virus prevalence of point 1 versus point 2 with the aim of establishing whether the presence of persisting polioviruses may have a pathogenic role in post-polio syndrome and of defining the peculiarities of genomic sequences of polioviruses detected in cases with post-polio syndrome as opposed to the genomic sequences of wild-type polioviruses.

Why look for poliovirus genome?

For many, the origin of post-polio syndrome is still poorly understood. Some do not question its origin, but attribute its consequences to living active lives with

bodies that have fewer nerves and fewer muscles. Time and age takes its toll. But, looking for an additional explanation makes sense.

Persistent poliovirus (PV) infection has been reported in individuals with B lymphocyte deficiency (and low or absent serum immunoglobulins; Li et al., 2014). Some evidence suggests that persistent PV infection could be associated with post-polio syndrome (Leon-Monzon et al., 1995; Baj et al., 2015).

Inflammatory changes in meninges, spinal cord and muscles have been reported (Ikemoto et al., 1996; Semino-Mora & Dalakas, 1998) and may suggest: persistent PV infection, autoimmune attack to central nervous system (CNS) targets, increased vulnerability of CNS to further infections.

What has been accomplished?

Polio patients have been seen by neurologists and appropriately diagnosed with post-polio syndrome (PPS) (or other forms of polio) using current diagnostic criteria (Farbu et al., 2011). Participants in the study have included PPS cases, stable polio cases, polio-free family members of PPS patients, non-polio neurologic controls and healthy blood donors.

What are some preliminary results?

Low-level genomes and infectivity *related to any one of the three PV types* have been detected at high frequency in PPS patients decades after the acute attack.

An additional conclusion of relevance to the field of public health (and also important for family members and co-workers of PPS cases) is that PV infection is not being transmitted from PPS patients to their family members.

Since effective treatments for PPS are still missing (Koopman et al., 2011),

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Left to right: Drs. Takashi Onodera, Konstantin Chumakov and Antonio Toniolo at National Institutes of Health discussing how to apply novel sequencing methods for examining poliovirus isolates of PPS cases.

identification of chronic PV carriers might indicate the need of treatment with human IgG or antiviral drugs/antibodies that are under development (McKinlay et al., 2015). Some treatments (Hu immunoglobulins) are currently under clinical trial in a multicenter international study.

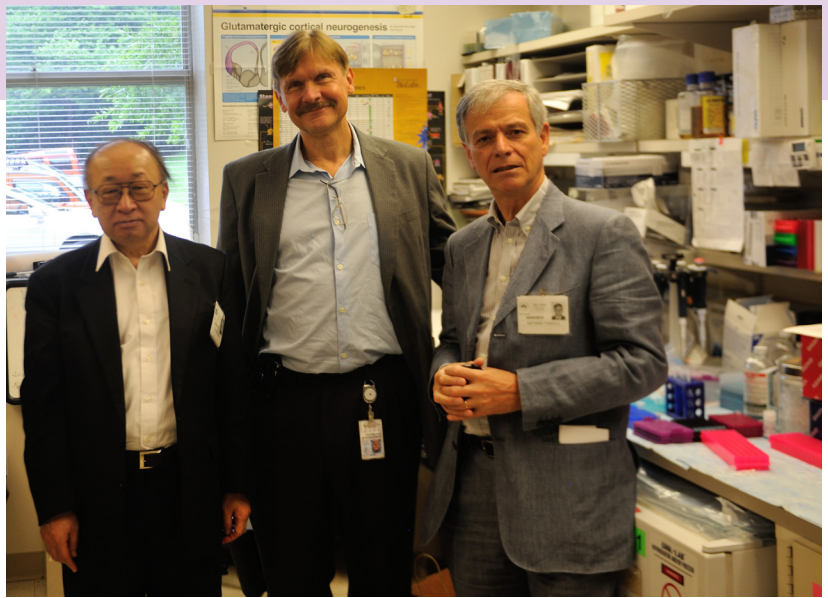
What are the team's next steps?

Select viruses isolated from PPS cases are being examined at the FDA in order to define the peculiarities of genomic sequences of polioviruses present in PPS cases versus those of wild-type polioviruses.

The recruitment of polio survivors with “stable polio” is continuing to extend the observations from the current to at least 30-40 cases.

The team will evaluate if anti-poliovirus antibodies may be effective in blocking the infectivity of poliovirus strains derived from PPS patients.

If positive, the results of the above tests will allow the team to propose “specific serotherapy” for treating PPS. In the meantime, they want to understand the possible role of poliovirus antibodies in the current therapy that is mainly based on the infusion of human immunoglobulins. ■



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