Genetically Unstable Renegade Cellular Sequences in Stealth Adapted Viruses

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Abstract

Certain classes of viruses have acquired cellular genetic sequences as part of their evolutionary formation. The acquired sequences have essentially become stable components within the virus. The incorporation of cellular sequences can also occur more dynamically as part of an immune evasion mechanism termed stealth adaptation. This involves the loss or mutation of genes coding for the relatively few components that are normally targeted by the cellular immune system. It has been shown to occur with cytomegaloviruses infecting the types of monkeys in which cultured kidney cells were used to produce live polio vaccines. Genetic sequencing of polymerase chain reaction (PCR) products generated in a selection of these viruses has revealed rhesus monkey-derived cellular sequences. Human cellular sequences were present in an African green monkey-derived stealth adapted virus. The human sequences have presumably replaced African green monkey cellular sequences by homologous recombination. Stealth adapted viruses need to be viewed as carriers of potentially highly pathogenic, genetically unstable "renegade" cellular sequences. As discussed in other articles, microbe-derived renegade sequences can also be present in stealth adapted viruses. These findings open a new era in potential virus-induced illnesses.

Key Words: Stealth adaptation, stealth adapted, renegade genetic sequences, polio vaccines, African green monkey simian cytomegalovirus, SCMV, rhesus cytomegalovirus, chronic fatigue syndrome, CFS, Long non-coding RNA, LncRNA, mental illness

Introduction and Discussion

Stealth adaptation refers to a viral immune evasion mechanism resulting from the deletion or mutation of the viral genes coding for the relatively few components, that are normally targeted by the cellular immune system [1-7]. It was initially described in a cytopathic virus cultured from a patient with chronic fatigue syndrome (CFS) [2]. Sequence analyses of this prototypic stealth adapted virus indicate the further acquisition of genetic sequences from cellular and bacterial genomes [8-15]. These additional sequences are seemingly abandoning their host in favor of further passage together with the remaining sequences of the originating virus. As such, they are referred to as renegade sequences [10-15]. Although the prototypic stealth adapted virus originated from an African green monkey simian cytomegalovirus (SCMV), the identified cellular-derived renegade sequences are from the human genome rather than from an African green monkey genome [10]. The likely explanation is that the African green monkey cellular sequences have been replaced by homologous recombination with corresponding human sequences. This conclusion is supported by sequencing data from the polymerase chain reaction (PCR) products generated from certain other stealth adapted viruses cultured from CFS patients. Of the five cultures from which PCR products were sequenced, three have cellular sequences derived from the rhesus monkey genome. In one of the cultures, four of the seven sequenced PCR products are rhesus in origin and the other three are of human origin [13-14]. Moreover, the human sequences have counterpart sequences in the rhesus genome [13-14].

Examples of the human-genome matching sequence from stealth virus-1 and a rhesus-genome matching sequence from stealth virus-3 are provided in Tables 1 and 2, respectively. Both sequences were generated using the same set of primers in the PCR. The primer sequences were excluded from the genetic analyses.

Cultured kidney cells from cytomegalovirus-infected rhesus and cynomolgus monkeys were used before the switch to African green monkeys in the production of poliovirus vaccines [16-21]. SCMV DNA is present in almost half of tested earlier polio vaccine lots produced from African green monkeys, while rhesus cytomegalovirus DNA is present in most vaccines produced in the cultured kidney cells of rhesus and cynomolgus monkeys [19-20].

Based on using various primers in the PCR, several of the partially analyzed cultured stealth adapted viruses are also derived from SCMV [3, 5]. Certain stealth adapted viruses have more likely arisen from human herpes simplex virus (HSV), Epstein Barr virus, and human adenovirus. There are also data supporting a possible HIV-derived stealth adapted virus. Based on research from others, enteroviruses may contribute to the formation of stealth adapted viruses, possibly even poliovirus. Thus, stealth adaptation is viewed as a generic process applicable to all viruses.

There are major implications regarding the sharing of cellular sequences between stealth viruses cultured from three unrelated individuals [13-14]. Rather than being a frequent and essentially random incorporation of renegade cellular sequences, this may be a relatively rare occurrence. Indeed, the incorporated sequence could possibly be involved in the virus regaining infectivity. To date, the incorporated cellular sequences are non-coding and positioned either within or between transcribed genes [10, 13]. In contrast, the incorporated bacterial renegade sequences correspond to at least parts of protein-coding genes [9-11, 13-14]. Various long non-coding RNA (LncRNA) cellular sequences are associated with the pathogenesis of specific illnesses [22-28]. This raises the possibility of certain stealth adapted viruses inducing specific illnesses attributed to their incorporated cellular sequences. While these could include known genetic diseases, they could manifest as entirely new disease entities.

Minor sequence variability is present between specific cell-derived renegade sequences in different individuals and even between the same originating cellular sequence in the virus cultured from the same individual. The variability results from nucleotide additions, deletions, or substitutions. The degree of sequence variability along with other data is consistent with RNA to DNA reverse transcription [29]. Generic instability of the cellular sequences could also change the pathogenicity of the virus. Identifying increased levels of a cellular sequence in pathological tissues, for example, a particular LncRNA sequence, is normally assumed to reflect an intrinsic genetic mutation. It could, however, reflect an infectious process.

It is of utmost importance to culture, isolate, and sequence stealth adapted viruses from human and animal populations. The culturing of stealth adapted viruses was deemed to be putting the Nation's health in "Immediate Jeopardy" [7]. This was undoubtedly due to the linking of these viruses to the inadvertent use of cytomegalovirus-infected monkeys in the production of polio vaccines [3, 16-20]. The determination was also precipitated by the positive cultures obtained from some individuals donating blood to a transfusion center. Prior to prohibiting further clinical testing, stealth adapted viruses were routinely being cultured from CFS patients, children with autism, adults with severe psychiatric illnesses, patients diagnosed as having chronic Lyme disease, and with other illnesses, including multiple myeloma [29-36]. Patient support groups do not wish to be burdened with the added concern of being potentially infectious to others. They do, however, pose occupational risks to others. There are also the risks of two-way virus transmissions between humans and animals.

Tentative evidence for virus transmission between individuals is provided by illnesses occurring within families [36]. A prime example is the occurrence of autism in children born to mothers with a prior or current history of CFS. Diverse manifestations of the illnesses among family members, such as those described in an earlier publication [36], could reflect minor changes in the infecting virus or preexisting disease susceptibility in the cross-infected family member. Some examples of caregiver burnout may also be attributed to acquired infections [36]. Occupational exposure to stealth adapted viruses is also to be expected, especially among human and animal healthcare providers, prison guards, schoolteachers, and other groupings of working individuals, such as orchestra players [29-40]. Disability tends to be more common among these groups, as unfortunately is suicide. Although numerous community outbreaks of CFS have been reported, Public Health officials have downplayed the likelihood of infection in favor of a hysterical reaction of wanting to be sick. This issue can most easily be settled by performing adequate virus cultures, sequencing of the viruses, and undertaking animal transmission studies. Public Health officials have been slow to respond to the published data on the first stealth adapted virus to be cultured from a CFS patient [2]. The second cultured virus was from a patient who was initially diagnosed with schizophrenia, but the diagnosis was later changed to bipolar psychosis [33]. Patients with mental illnesses deserve to know if a stealth adapted virus infection is contributing to their illness. As will be discussed in a subsequent article, means are available to suppress stealth adapted and indeed all viruses via the alternative cellular energy (ACE) pathway [41-43].

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Table 1. Nucleotide Matching Showing Human-derived Cellular Sequence in PCR Product from Stealth Adapted Virus-1

Species	**NCBI accession**	**Identical Nucleotides**	**% Identity**	**Gaps**
Human	**NC_000023.11**	**606/609**	**99.51**	**2**
Rhesus Monkey	**NC_041774.1**	**555/609**	**91.13**	**5**
African Green Monkey	**NC_023671.1**	**553/609**	**90.80**	**2**
Chimpanzee	**NC_036902.1**	**598/609**	**98.19**	**2**

Table 2. Nucleotide Matching Showing Rhesus Monkey-derived Cellular Sequence in PCR Product from Stealth Adapted Virus-3

Species	**NCBI accession**	**Identical Nucleotides**	**% Identity**	**Gaps**
Human	NC_00008.11	447/505	88.51	16
Rhesus Monkey	NC_041761.1	504/510	98.82	3
African Green Monkey	NC_023649.1	478/508	94.09	4
Chimpanzee	NC_036887.1	444/505	87.92	16