Currently recommended treatment regimens is feasible and effective in intravenous drug users (IDU). Treatment of HCV in IDU with current recommended treatment regimen (standards of care) through consulting services offered by two community-based clinics in British Columbia. Some received treatment in correctional institutions either entirely or at some time during the course of treatment. The treatment was however supervised by the two community based clinics.

**Results:** 585 individuals: 88.2% males (516/585) mean age 40.6 ± 9.01, 11.8% females (69/585) mean age 42.0 ± 9.52. Of those with relevant data, 74.7% (437/585) were treated in prison, 25.3% (148/585) were treated in the community. Total admitted IDU history 100% (585/585). SVR (ITT analysis) by genotype: Geno 1: 44.9% (150/334); Geno 2: 71.4% (40/56); Geno 3: 83% (140/188); Other Genotypes: 57.1% (47). Re-infection occurred in 14.2% (62/437); Reinfection was more likely to occur amongst inmates (or former inmates) 1.4% (2/148) in non-inmates, P=0.001, OR 11.82, CI Lower 3.1 and CI Higher 101.3. 3.2% (19/585) deceased.

**Conclusion:** Treating HCV amongst IDU is feasible and effective. SVR rates were consistent with non-IDU populations. Genotypes 2 & 3 had higher rates of SVR than genotype 1. Re-infections occurred mostly in inmates of correctional institutions. Addressing addiction is important before, during and after treatment is important for maintenance of SVR. 3.2% of individuals we followed died. This number is likely underestimated as many were lost to follow up. Efforts must be made to reach and treat vulnerable populations sooner to prevent further spread of disease and increase treatment success. Successful treatment programs for HCV in IDU must include on-going management of addictions, and regular health-care engagements.

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**Epidemiological significance of non-glycosylated Asn residues found in the hemagglutinin protein of the H1N1 influenza virus from 1918 to 2012**

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**Background:** Influenza A virus hemagglutinin (HA) consists of a head (HA1) and stem (HA2) where certain non-glycosylated asparagine (Asn) residues contribute to protein stabilization and to overall protein conformation which can influence both the evolution and pathogenicity of the influenza virus. This suggests that non-glycosylated Asn residues play a significant role in HA, making it a good focus for epidemiological studies, however, no study have been made to date.

**Methods:** We analyzed 2,830 H1N1 HA sequences and focused our study on non-glycosylated Asn415/416 and Asn472–473 residues found within the H1N1 strains circulating through 1918–2012. Frequency of Asn residues originating from human, avian and swine were established. We used the I-Tasser, HCA and Phyre
2 softwares to predict the protein conformation and hydrophobicity. 3D structures with the highest C-score were considered. We looked at the different HA conformations in the presence or absence of non-glycosylated Asn415/416 and Asn472–473 residues and correlated this with influenza transmission patterns and pathogenicity.

**Results:** Through 1918-2012 we found that non-glycosylated Asn residues are conserved at the amino- and carboxyl-terminal region of the 53-residue long alpha-helix uniquely found in HA2. We found that the amino-terminus will either have a single Asn residue or an Asn-Asn doublet whereas the carboxyl-terminus will always have an Asn-Asn doublet. Interestingly, we found that whenever Asn415-Xxx416 (where X is any amino acid residue) is the same in two species, HA1 conformation is the same and interspecies transmission of the virus occurs. Moreover, whenever a shift from a single Asn415 residue to an Asn415-Asn416 doublet or vice-versa occurs in the amino-terminus, it results to significant structural changes in HA1 which surprisingly coincides with the 1918 Spanish flu, 1977 Russian flu and 2009 Swine flu. Structural analyses using the 2009 HA show that mutations at either Asn415 or His416 has no change in HA1 conformation, however, when both were changed, HA1 conforms to the 1977 HA. Similarly, we observed that mutations at Asn472, Asn473 or both results into the 1977 HA.

**Conclusion:** Non-glycosylated Asn415 and Asn472-Asn473 doublet can influence HA1 conformation. In addition, Asn415-Xxx416 pairs can determine interspecies transmission and pathogenicity of the H1N1 influenza virus.

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**Nucleic acid-based drugs against the highly pathogenic H5N1 avian influenza virus infection**

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**Background:** Highly pathogenic H5N1 avian influenza virus (HPAIV) continues to cause serious global concerns because it threatens the poultry industry and causes loss of human lives. The ability of HPAIV to mutate and develop resistance to antiviral drugs and vaccines necessitates the development of novel drugs and vaccines, including those which are nucleic acid-based. Liposome-encapsulated Poly ICLC (a ds RNA and a toll-like receptor-3 [TLR-3] agonist) and antisense oligonucleotides are examples of nucleic acid-based drugs which can be safe and efficacious against HPAIV.

**Methods:** Using a lethal Balb/c mouse model, liposome-encapsulated Poly ICLC and antisense oligonucleotides (directed against the hemagglutinin protein) were evaluated for their prophylactic or therapeutic efficacy against a wild strain (influenza A/H5N1/chicken/Henan/2005) of HPAIV. Liposome-encapsulated Poly ICLC were administered intranasally at day -3 and day -1 prior to HPAIV challenge, and antisense oligonucleotides were administered intranasally at 4 and 8 hours post virus challenge. Antiviral efficacies were determined by comparing the survival rates of drug-treated mice at day 14 post infection compared to control saline group.

**Results:** Depending to various challenge doses of HPAIV, liposome-encapsulated Poly ICLC administered intranasally provided 67–100% protection when given at up to 24 and 48 hrs prior to virus challenge. RT-PCR analysis of lungs tissues of LE Poly ICLC treated mice indicated up-regulation of TLR-3 and antiviral interferons (-α, -β and -γ) mRNAs production. Treatment of mice with antisense oligonucleotides administered to mice at 4 and 8 hours post infection were completely protected against a 10 lethal dose virus challenge with influenza A/H5N1/chicken/Henan/2005, or with influenza A/PR/8/34 (H1N1). However, therapeutic efficacy of antisense oligonucleotide decreased when treatment with antisense was delayed beyond 8 hours post infection.

**Conclusion:** Liposome-encapsulated Poly ICLC provided high level of protection in mice against lethal doses of HPAIV, and against a seasonal strain of influenza A/PR/8/34 virus (H1N1). Activation of TLR-3 signaling pathway can provide broad-spectrum protection against various strains of influenza virus, regardless of mutations. Post-exposure treatment of HPAIV can be achieved through silencing of influenza virus gene expression using virus-specific antisense oligonucleotides. These findings support the potential role of nucleic acid-based drugs for prevention and treatment of HPAIV.

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**SARS-Coronavirus ancestor’s foot-prints in Thai bat colonies and the refuge theory: A phylogeography perspective**

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**Background:** Elucidating relations between viruses and their hosts remains one of the great challenges of the ecology of infectious diseases and may help in identifying drivers of emergence of new pathogens. Following the emergence of SARS, several studies have pointed out the great diversity of Alphacoronavirus and Betacoronavirus in bats as well as the existence of SARS-related-CoV infection in apparently healthy bats. To date, the greatest Coronavirinae diversity has been observed in Microchiroptera and the closest wild virus to SARS-CoV has been detected in this group as well, and more precisely in the Rhinolophoidea super-family. The Rhinolophidae were firstly recognized to host SARS-CoV related Coronavirinae and therefore were the most represented bat family in the sampling record. Consequently, their sister group, the Hipposideridae, were less considered in studies focusing on Coronavirinae ecology. Given the phylogenetic proximity of these two bat families, their broad and partially sympatric repartition and their diversified behavior, we hypothesized that they might both harbor betacoronaviruses related to SARS-CoV in Asia and that the study of their phylogeny may help to understand the genesis of SARS-CoV.