Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

P89 Combined anti-influenza virus effect of a plant polyphenol-rich extract and rimantadine

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Background: The anti-influenza virus activity of the polyphenol-rich extract from *Geranium sanguineum* L (PC) has been studied intensively. Its in vitro virus-inhibitory effect was strain-dependent; PC inhibited the virus-induced cytopathogenic effect and plaque formation, the production of infectious virus and haemagglutinin, the synthesis of virus-specific RNA and proteins (Serkedjieva and Hay, 1998). PC protected mice from mortality in the experimental influenza A/Aichi/2/68 (H3N2) virus infection (EIVI) (Serkedjieva and Manolova, 1992).

Results: The in vitro combined use of PC with Rimantadine hydrochloride (Rim) resulted in synergystic inhibition of the A/chicken/Germany/34, strain Rostock (H7N1) virus replication in MDCK cells. The cooperative effects were defined on the base of infectious viral yields by two complementary methods. The joint application of PC and three other amantadine derivatives also resulted in marked enhancement of inhibition. Administration of PC in combination with Rim in the EIVI in mice produced a synergistic protective effect: mortality rates were significantly decreased (index of protection = 77.8%), mean survival times were markedly prolonged (+5.2 days). A pronounced reduction of the lung lesions due to infection and of lung infectious virus titres was achieved ($\Delta \log_{10} TCID_{50}$/ml = 1.6–2.4).

Discussion: While the need for novel potent antiviral agents continues to exist, the strategy of combined antiviral therapy with available antiviral drugs has proved its usefulness. The presented results suggest that the combined use of natural and synthetic viral inhibitors may be used successfully to potentate the antiviral efficacy of the plant preparations and may enable dose reduction of their toxic components.

P90 Inhibition of HCoV-NL63 infection at early stages of the replication cycle

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Background: HCoV-NL63, a recently discovered member of the Coronaviridae family, has spread worldwide and is associated with acute respiratory illness in young children, elderly and immunocompromised persons. Further analysis of HCoV-NL63 pathogenicity seems warranted, in particular because the virus uses the same cellular receptor as SARS-CoV.

Methods: As there is currently no HCoV-NL63 specific and effective vaccine or drug therapy available, we evaluated several existing antiviral drugs and new synthetic compounds as inhibitors of HCoV-NL63, targeting multiple stages of the replication cycle.

Results and Conclusions: Of the 27 compounds that we tested, five potently inhibited HCoV-NL63 at early steps of the replication cycle: Intravenous immunoglobulins (IVIG), heptad repeat peptides, siRNAs, beta-D-N4-hydroxycytidine and 6-azauridine. These compounds showed low IC50 values and low cytotoxicity and are candidates to be developed further for mono- or combination therapy.

P91 Prevalence of two recently described HBV mutations and their effect on adefovir therapy

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Background: Adefovir dipivoxil is licensed for the treatment of patients with chronic hepatitis B infection particularly those with lamivudine-resistant HBV infection. A minority of HBV infected patients respond poorly to Adefovir treatment while others develop resistance. There are two known mutations, A181V and N236T, that mediate resistance but recently two additional primary mutations L217R and I233V have been reported to be associated with Adefovir resistance.

Aims: To investigated the prevalence of the L217R and I233V mutations in a cohort of patients chronically infected with HBV and treated at the Liver Unit, Queen Elizabeth Hospital, Birmingham, UK.

Methods: HBV sequences from samples sent to our laboratory between January 2003 and December 2005 from patients on antiviral therapy were examined.

Results: Samples from 36 patients were reviewed. The majority were genotype A (47%) and genotype D (31%). Lamivudine associated mutations were detected in 25 samples. L217R mutation was detected in 10 patients (28%), all infected with genotype A and in 9 cases Lamivudine associated mutations were also detected. 6 of the patients received Adefovir therapy and all responded virologically, some up to 2 years. To date no other Adefovir associated mutations have been detected in any of the patients. None of the 36 patients had the I233V mutation.

Conclusion: The L217R mutation was detected in 59% of our genotype A samples and does not seem to be associated with a poor response to Adefovir.

P92 Naturally-occurring hepatitis C virus protease variants: implications for resistance to new antivirals

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Background: Recent publications have identified, in the replicon system, amino acid mutations in the HCV protease associated with resistance to new HCV protease inhibitors. However, there is little information in the literature on the natural variability of proteases from the different HCV subtypes.

Aims: To determine the natural variability on HCV proteases both within and between different viral subtypes and to compare it with known mutations conferring resistance to protease inhibitors.

Methods: Data mining on the EuHCVdb and Los Alamos HCV databases. A total of 211 non-redundant full-length HCV NS3 sequences were selected (159 genotype 1, 35 genotype 2, 17 genotypes 3, 4, 5 or 6). Amino acid frequencies were calculated to each position using VESPA and variation in sites potentially associated with resistance to protease inhibitors BILN-2061, VX-950, SCH-503034, and SCH6 were then compared to the HCV Con-1 protease sequence.

Results: Sequence heterogeneity was frequent in compensatory-mutation sites, such as T72, P89 and specially Q86 (Q86P in all non-genotype 1, and in 30% of genotype 1 sequences). BILN-2061 resistance-associated D79E was present in almost all genotype 2 sequences, thus validating our analysis. T54A, R109K, A156T/V/S, D168V/A/Y, or V170A (associated to BILN-2061, VX-950, or SCH-503034 resistance) were not observed, except for one genotype 6 isolate carrying V170A. New variations with unknown effect in resistance were common, such as D168E (in genotype 1 isolates) and V170I (in 45% of genotype 1 and in almost all non-genotype 1 sequences). Furthermore, 14% of subtype 1b isolates carried I153V, potentially implicated in low-level resistance to SCH6.

Conclusions and Discussion: There is relevant sequence heterogeneity in the NS3 protease of natural HCV isolates from different viral subtypes, with potential implications in HCV resistance to protease inhibitors. These data may be very useful for future genotypic testing before and during new antiviral treatments.

P93 Amantadine resistance among influenza A isolates in Sweden 2001–2006

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Adamantanes (amantadine and rimantadine) can be used as prophylaxis or treatment of Influenza A infections. These matrix protein 2 blockers prevent release of the viral RNA in the cell. Recent