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Structure-based chemotherapy of SARS - where do we stand, three years after the global outbreak?

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Three years have passed since the global outbreak of severe acute respiratory syndrome (SARS). During this time, major progress has been made in understanding the mechanisms of infection [1]. Three-dimensional structures have been determined for a number of non-structural and structural proteins of the virus and of related coronaviruses [2-5]. In the absence of a crystal structure for the viral RNA polymerase, the main proteinase remains the most suitable anti-coronaviral drug target [3,6-10]. Progress in designing and synthesizing specific inhibitors for this enzyme will be reported.

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Crystal Engineering of Porphyrin Network Materials

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The chemical and structural diversity of porphyrins allows us to reasonably control their self-assembly process and to alter systematically the composition, topology, porosity and functionality of the crystalline supramolecular arrays that form. Application of this crystal engineering approach to the systematic development of open chiral as well as achiral environments are of particular interest, as such porous architectures, which sustain large amounts of void space, can be used in selective inclusion, storage and transport processes and in catalyzed molecular transformation reactions. It represents an attractive "*bottom-up*" strategy to tailoring ordered lattice-materials and organic zeolite analogs from tetraarylporphyrin (TPP) building blocks. Typically, the square-planar functionality of the TPP framework or of its metallated analog (M-TPP) is ideal for fabrication of flat arrays, when incorporation of molecular recognition features on the porphyrin periphery preserves the square-planar symmetry to allow multiple and divergent intermolecular associations. The latter can be either nucleophiles capable of coordinating to metal centers, or groups with complementary hydrogen-bonding capacity. Correspondingly, we have assembled a variety of 2D porphyrin networks either by direct hydrogen-bonding, or by utilizing external bridging auxiliaries as metal cations, inorganic anions and organic ligand linkers [1, 2].
Crystal engineering of 3D multi-porphyrin frameworks can be also approached and achieved in several ways [1, 2]. This includes direct self-assembly of suitably functionalized metalloporphyrin entities through coordination, tessellation of peripherally functionalized TPPs by ionic (single metals, metal clusters or metal complexes) bridges of tetrahedral or octahedral coordination directionality, and formulations assisted by organic ligands. These efforts afforded framework solids with easy to tailor grid sizes that resemble molecular sieve type materials. Designs of chiral architectures can be based on porphyrin units decorated with mixed functional groups that exhibit reduced $C_2/C_{2v}/C_{4v}/D_4$ point symmetry, in relation to D_{4h} porphyrin derivatives with symmetrically substituted functions. The possibility to bias the intermolecular organization of inherently achiral porphyrin species by directed self-assembly, to form non-centrosymmetric network structures, will be demonstrated [2, 3]. Issues of supramolecular isomerism in the porphyrin network materials will be addressed as well.

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