isomorphous with the I-Phe-Tyr-NH_2 complex, the four crystallographically distinct neurophysin molecules were found to associate into an elongated tetramer consisting of two similar neurophysin dimers. However, in contrast to the structure of the I-Phe-Tyr-NH_2 complex, in which the neurophysin tetramer was found to contain five dipeptide molecules, the native neurophysin tetramer contains only four bound dipeptide molecules. A full crystallographic refinement using XPLOR is underway. The current R factor is 20.1%. Details of the structure determination as well as analysis of the structure will be presented.

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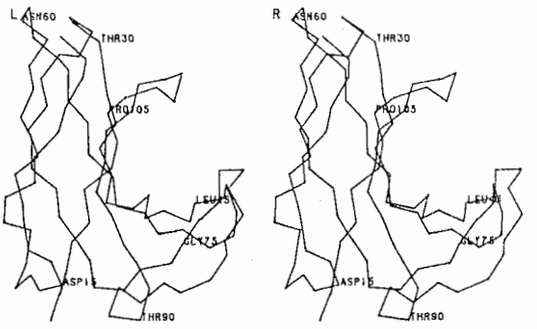

PS–03.11.14 REFINEMENT AND INTERPRETATION OF THE X-RAY STRUCTURE OF APO-NEOCARZINOSTATIN AT 1.8Å RESOLUTION. by M.Ramanadham*, Solid State Physics Division, Bhabha Atomic Research Centre, Trombay, Bombay 400085, India, and Larry C. Sieker, Department of Biological Structure, University of Washington, Seattle, WA 98195, USA

Apo-neocarzinostatin (apo-NCS), the 113 amino-acid long polypeptide component of the antitumour, antibiotic protein neocarzinostatin (NCS), has been refined at 1.8Å resolution by the method of stereochemically restrained least-squares. (Sp.gr. $P2_12_12_1$, a=27.36, b=33.89, c=101.9Å, Z=4). Prior to this, the structure was refined at 2.25Å resolution to an R-value of 0.37 for a model consisting of 751 out of 778 protein atoms. Numerous difficulties encountered in extending this refinement further had taken us back to the MIR map. A thorough re-examination of this map resulted in a model, which is consistent with not only the electron density distribution, but also the accepted rules of conformation and inter-atomic interactions. Further model improvements were affected by the use of Fourier maps phased by the atomic positions obtained during the previous step. Refinement and periodic model editing at 2.25Å resolution, commenced only after the conclusion of these steps, had resulted in an R-value of 0.27. The data were then extended to 1.8Å resolution (7,559 observations in the d-spacing range 10-1.79Å), and refinement was continued, eventually leading to a model consisting of all the 778 protein atoms and 248 solvent atoms with an R-value of 0.155. The final model is completely unambiguous in terms of the Fourier map interpretation, and is quite satisfactory from the point of view of structural and stereochemical considerations. A detailed analysis of the structure, conformation, and the chromophore binding site has been carried out. This model is currently in use for interpreting the binding of ethidium bromide to NCS at 2.5Å resolution. Efforts are also underway to model the chromophore binding to NCS at 2Å resolution.

PS–03.11.15 CRYSTALLISATION AND X-RAY DIFFRACTION STUDIES OF RECOMBINANT HUMAN PLATELET-DERIVED ENDOTHELIAL CELL GROWTH FACTOR
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Thymidine phosphorylase (TP) is one of two pyrimidine phosphorylases in the base and nucleoside salvage pathway. A search of the NBRF-PIR sequence database has revealed a striking homology (40% identity over 438 aligned positions) between TP derived from *E. coli* and human platelet-derived endothelial cell growth factor (PD-ECGF) (Barton *et al.* , 1992). This strongly suggests that human PD-ECGF is identical to human TP. PD-ECGF is known to stimulate the growth and chemotaxis of endothelial cells *in vitro* and possesses angiogenic activity *in vivo*. It is likely that endothelial cells respond specifically to a modulation in intracellular DNA precursor pool brought about by thymidine phosphorolysis.

Five different crystal forms of recombinant human PD-ECGF from yeast were produced from initial screening of crystal growth parameters using the "magic fifty" set of conditions (Jancarik & Kim, 1991) and the hanging drop vapour diffusion technique (Hampel *et al.*, 1968) One of the forms proved suitable for X-ray analysis. These crystals belong to the space group $P2_12_12_1$ with unit cell dimensions a=63.7 b=70.4 c=219.6 Å $\alpha = \beta = \gamma = 90°$. Assuming a 47% solvent content the crystals contain a single dimer in the asymmetric unit . A set of diffraction data has been obtained using station X11 of the Hamburg synchrotron source which is 84% complete at the 1σ level to 3.5Å Bragg spacings.

PS–03.11.16 CRYSTAL STRUCTURE ANALYSIS OF HUMAN DIHYDROFOLATE REDUCTASE INHIBITOR COMPLEXES. Vivian Cody*, Joseph R. Luft, Erik Jensen, Walter Pangborn, Andrzej Wojtczak, Nikolai Galitsky, J.H. Freisheim[!] and R. Blakley[+], Medical Foundation of Buffalo, Buffalo, NY 14203, [!]Medical College of Ohio, Toledo, OH 43699, [+]St. Jude Children's Hospital, Memphis, TN 38101.

Data from a methotrexate (MTX)-resistant human cancer cell line reveal a natural F31S mutation in the enzyme dihydrofolate reductase (DHFR). Kinetic data for F31 mutants shows greater effects on binding for folates than antifolates. To understand the structural basis for selectivity and specificity for binding to DHFR, and to determine the fundamental role of F31 in binding and catalysis, we have co-crystallized a series of antifolate inhibitors with both human wild type and F31 mutant DHFR as binary and ternary complexes with the cofactor NADPH. We report structural data for isomorphous R3 crystal complexes with anti-

