DNA TOPOISOMERASES IN THERAPY

THE FOURTH CONFERENCE ON DNA TOPOISOMERASES IN THERAPY

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New York University Medical Center
350 First Avenue
New York, New York 10016

GENERAL INFORMATION

CONFERENCE DIRECTOR
Walter Perlmutter, M.D., Ph.D.

CONFERENCE LOCATION
NYU Medical Center
Alumni Hall Auditorium
550 First Avenue (at 30th Street & 1st Ave.)
New York, NY 10016

INFORMATION
Registration Office
NYU Post-Graduate Medical School
550 First Avenue, New York, NY 10016
(212) 252-5295

TUITION FEE — Pre-registration required. Tuition is $200 payable when submitting application. Prince is a reduced fee of $150 for Ph.D. or M.D. candidates and post-doctoral trainees upon written confirmation from their Chief of Laboratories of Service. Enrollment is limited and applications will be accepted in the order of their receipt. An early pre-registration is encouraged.

WITHDRAWALS — There is a 20% cancellation charge for withdrawals. All requests must be in writing and postmarked no later than October 12, 1992. There will be no refunds after this date. In the unlikely event that this Conference is canceled, all payments will be returned in full.

ACCREDITATION — The NYU Post-Graduate Medical School is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor continuing medical education for physicians.

Graduate Medical School designates this continuing medical education activity for 26 credit hours in Category 1 of the Physician’s Recognition Award of the American Medical Association. Of your attendance will be maintained by the Post-Graduate School for six years from the starting date of the course.

HOTEL ACCOMMODATIONS — Subject to availability, there are special rates for registrants in this course. Information and hotel reservation cards will be sent with confirmation of enrollment. Since rooms are in heavy demand throughout the year, please contact the hotel early in order to secure your reservation.

PARKING — Parking is available at the Kips Bay Parking Garage directly across from the Medical Center at 571 First Avenue. There is additional parking on 30th Street between First and Second Avenues.

NEW YORK CITY — In each pre-registration packet information is provided to assist your access to New York City’s cultural and entertainment facilities including a THEATER TICKET SERVICE CONTACT. Your hotel can be helpful concerning tickets to theaters, concerts, ballet, museums and athletics events.

TRANSPORTATION — Our travel agent, ZENITH TRAVEL, INC., has negotiated special discounted fares that will result in savings of 5% to 15% from most cities. To take advantage of these savings, call ZENITH at 800-221-2785 (NYS residents call 212-963-0012) between the hours of 9:00 a.m. and 5:00 p.m. EST and identify yourself as an NYU medical summer participant. Having your credit card available will facilitate the reservation procedure.
DNA GYRASE: THE MOLECULAR BASIS OF QUINOLONE AND COUMARIN DRUG ACTION.
Anthony Maxwell, Asunción Contreras and Christopher J.R. Willmott. Department of Biochemistry, University of Leicester, Leicester LE1 7RH UK.

DNA gyrase is the bacterial enzyme which catalyses the introduction of negative supercoils into DNA using the free energy of ATP hydrolysis. The enzyme from E. coli consists of two proteins, A and B, of molecular weights 97 and 90 kDa; the active enzyme is an A2B2 complex. Gyrase is the target of the quinolone and coumarin antibacterial agents, which are both effective inhibitors of the DNA supercoiling reaction. However, the molecular basis of the action of both groups of drugs is incompletely understood.

Using a spin-column binding assay, we have found that the quinolone drug norfloxacin binds to the gyrase-DNA complex but not to either the enzyme or DNA alone. If the gyrase A subunit carries the mutation Ser83→Trp (which confers quinolone resistance), then binding to the gyrase-DNA complex is abolished, implicating this residue in enzyme-drug interaction. In addition, we have investigated transcription in vitro in the presence of gyrase and quinolone drugs. We have found that either gyrase or quinolone drugs alone have no effect, but in combination lead to blockage of transcription. Gyrase containing the mutation GyrA(Ser83→Trp) does not affect transcription in the presence of quinolone drugs. These experiments suggest a possible model for the effect of quinolone drugs in vivo.

With respect to the coumarin drugs, we have sequenced the gyrB genes in a number of spontaneous coumermycin-resistant E. coli strains. The mutations occur at residue Arg136, which is altered to Cys, His or Ser. We have also mapped a chlorobiocin resistance mutation to Gly164 (to Val). In relation to the known structure of the N-terminal fragment of the gyrase B protein, these mutations map close to, but not within, the ATP-binding site. We have produced GyrB proteins bearing these mutations and studied their properties in vitro.