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The 46th meeting of The American Society of Tropical Medicine And Hygiene, Coranado Springs Resort, Florida. 7-11 December 1997.

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A contribution of £200 from the James Rennie Bequest enabled me to attend the 46th annual meeting of The American Society of Tropical Medicine And Hygiene. The meeting, one of the largest parasitological conferences in the world, consisted of 37 scientific sessions, 22 symposiums, 2 poster sessions and 4 Plenary Lectures. During the 5 day meeting I presented a 15 minute talk on my PhD project and chaired the scientific session: Filarial Molecular Biology, a 4 1/2 hour session containing 9 talks.

The tremendous breadth of the meeting provided an excellent opportunity to attend scientific sessions on a wide variety of subjects. Sessions on protozoa and clinical filariasis in particular made important impact on my current project and my future career plans.
The meeting also allowed me to meet with labs that I have collaborated with in the past and to discuss the possibility of working in labs in the US. During the meeting I was offered the possibility of work in two american universities.

Collaborations initiated
An important aspect of my project involves the elucidation of the possible functions of the genes I have characterised. It is therefore critical to know whether the protein products are secreted from the nematode as excretion presents the possibility that these proteins have an extracellular function, acting on host molecules in order to promote parasite survival in the host in the face of a vigorous attack from immune system. After my talk a group from the School of Public Health, Johns Hopkins University, Baltimore, MD, USA. proposed a collaboration to detect my proteins in the supernatants of cultured parasites at different stages of their life cycle using antiserum to recombinant proteins.

Overview of the meeting
Although the meeting was broad in it's gathering of more than 3,00 people from an enormous variety of disciplines from clinical medicine to pure molecular and cell biology it could not go unnoticed that the most prominent disease at the meeting was malaria, reflecting the morbidity caused by these parasites, the wealth of knowledge being gathered on this disease and , after attending many of the sessions, how much is still to be learned. Many talks were concerned with the development of a vaccine, a

area still in it's infancy despite claims of moderately significant efficacy of the Spf 66 vaccine in clinical trials.

Some of the work more interesting to me and more relevant to my field was the report of studies on the cell biology of malaria in the mosquito vector. Mohammed Shahabuddin, NIH, Bethesda, presented evidence that the parasite targets a particular class of cells within the midgut epithelium of the vector mosquito which enable them to move out of the mosquito midgut after a bloodmeal. High resolution confocal microscopy graphically demonstrated that the parasite binds to a minority of cells contained with the midgut epithelium and use these cell to cross the epithelium. These cell exclusively express vacuolar-ATPase and this was used as a marker for these cells. Understanding the function of these cells and there role in the transmission malaria would help in the development of strategies to block transmission at a point in the parasites life cycle where it is not able to vary it's life cycle strategies to the same extent as it does within it's human host.

Another important talk for me was a keynote speech given by Eric Ottessen from the WHO Geneva. He reported on the results of clinical trials carried out at a number of centres around the world using a double drug treatment regime against human lymphatic filariasis. Significantly they found that giving the drugs on a yearly basis was as effective as monthly or three monthly doses. These were important studies not only because yearly doses reduce the cost of treatment but the inclusion of two drugs with different antiparasite targets would theoretically reduce the risk of drug resistance emerging in the future.
Other important talks within my field were the reporting of new nematode molecules with potentially important functions. Al Scott, Johns Hopkins University, Baltimore, reported on the functional characterisation of a filarial protein with homology to human macrophage migration inhibitory factor. This was functionally expressed in *E. coli* and shown to prevent the accumulation of monocytes and granulocytes around parasites *in vitro*. This was an important example of how parasites could potentially evade one arm of the host's immune response. Further insights into nematode biology were given by Ramaswamy Chandrashekar, Heska Corporation, Colorado, who described the cloning of transglutaminase, a molecule shown to be important in the biosynthesis of the nematode cuticle. Inhibitors of transglutaminases are selectively lethal to nematodes and represent a novel chemotherapeutic target. The functional expression of a filarial transglutaminase revealed that this molecule not only has transglutaminase activity but was able to catalyse the isomerisation of intramolecular disulphide bonds, commonly found within the cuticular collagens of nematodes, pointing to a pivotal role for this molecule the growth and maturation of filarial parasites.

Oral presentation presented at the meeting:

Characterisation of genes highly expressed in larval *Brugia malayi*

William Gregory, Mark Blaxter and Rick Maizels

Larval *Brugia malayi* recovered from vector mosquitoes 10-14 days after infection lie dormant until transmitted to a human host. In order to identify genes important for the survival of the larvae (L3) in the mosquito or transmission to their mammalian host we have performed RT-PCR on L3 RNA using nematode spliced leader and oligo-dT primers followed by cloning of the most abundant products. Separation of the products on agarose gels revealed a limited number of intense bands, many of which were not present in similarly treated RNA extracted from larvae 9 days after infection of gerbils. These bands were excised, cloned and sequenced. The predicted protein products of the genes identified include a cystatin-type cysteine protease inhibitor (*Bm-cpi-1*), a homologue of a *Dirofilaria immitis* 20/22kDa protein (*Bm-alt-1*) and a homologue of the recently identified mammalian histamine releasing factor (*Bm-tph-1*). The predicted mature protein products of these genes have be cloned into pET 29 and expressed as His-Tagged fusion proteins.

Additionally, a gene showing 26% identity to *cpi-1* has been identified through EST sequencing by the Filarial Genome Project. The full length sequence of this gene, designated *Bm-cpi-2*, has been obtained and the predicted mature protein expressed. Both recombinant *cpis* inhibit the cleavage of fluorescent peptide substrates by cysteine proteases.

Antisera to recombinant *cpi-1*, *cpi-2* and *alt-1* immunoprecipitate molecules present in surface labelled L3 preparations although they fail to bind to the surface of live, intact L3s. Antiserum to *cpi-2* also precipitate molecules from surface labeled adult preparations and excretory-secretory products.