Congress Interviews

Find out more about about the EHA Congress through our interviews with members of the various committees required to help run it.

Featuring: Professor Shai Izraeli, Doctor Marek Mraz, and Professor Barbara Bain.

Professor Shai Izraeli

Treasurer of EHA Executive Board and Director of the Division of Pediatric Hematology and Oncology, Schneider Children's Medical Center, Petah Tikva, Israel

Q1

You are the treasurer of the executive committee for the European Hematology Association (EHA). How do you prioritise and delegate the funding which is provided to the EHA and use it in the most effective way possible?

The board and the committees of the EHA are working on an investment plan for the next 3 years. Our two major goals are to support education and research of haematology in Europe and beyond. The process ensures the incorporation of diverse ideas generated by many members of EHA committees.

Q2

How do you find time to juggle your responsibilities with the EHA and your roles outside the association, most notably as the Director of the Pediatric Hematology Oncology Division in Schneider Children's Medical Center of Israel.

This is indeed challenging but there is a saying: if you want something to get done, give it to a busy person. I am fortunate to have fantastic assistance both in my main activity as the head of a very large clinical paediatric haematology oncology department and the activity in the EHA. One can do quite a bit in 24 hours each day.

Q3 As an Executive Board Member, you can directly influence how the EHA operates. How important is communication between the different committees towards fulfilling the association's main objectives and ensuring the best congress possible?

Communications are critical indeed. Committee chairs are often invited to board meetings and many chairs are board members. In addition, we established two committees: the education and research committees that oversee most of the other committees in the two most important fields in the EHA – promoting education and research towards better clinical care of patients with haematological disorders. In addition, we are in direct contact with the Scientific Working Groups – which are groups organised by the European haematology community usually around a disease topic (such as myeloma and chronic lymphocytic leukaemia). Finally, we interact with the national haematology associations. All these communications ensure that EHA is a true representative of haematology in Europe.

"This is the field that pushes the envelope. Problems and unmet needs of patients are taken to the laboratory where new discoveries are made that are quickly translated to the clinic and change patients' lives."

Q4 Education is clearly a key focus of the EHA. Can you explain how the association decides on and assimilates the content that is provided across the various platforms on your website (e.g., Master Class and Hematology Curriculum)?

The education committee is one of the most active committees in the EHA. In addition to the web content EHA conduct training that focusses on young haematologists and haematologist scientists. This focus on 'YoungEHA' includes a course on Translational Research Training in Hematology (TRTH), a joint initiative with the American Society of Hematology (ASH), and Clinical Research Training in Hematology (CRTH). The goal of both programmes is to train the future basic and clinical researchers in haematology.

Q5 Your professional career spans three decades, the majority of which has been spent in research institutes in either Israel or North America. Are there striking differences or similarities that you can comment on regarding the outlook and emphasis you have experienced in these institutes?

Basically, I was in two types of institutions: I was trained in the NIH National Cancer Institute USA. This is a unique place, in that it is the only one in the world that is devoted to both basic translational and clinical research. There is no emergency room in the NIH. It is highly selective, admitting and treating only patients who enrol on specific clinical research protocols. The budget is almost unlimited, and one does not have to apply for grants. Hence the NIH is the place for ground-breaking research.

In Israel I have been working in public academic hospitals; most recently, I head up the Division of Pediatric Oncology in Schneider Children's Medical Center: a major referral centre for children with cancer and serious haematology disorders. We do not select patients, we serve everyone. We combine superb clinical care with advanced diagnostics and research. We do not have the financial means of the NIH. Moreover, in the last 19 years, since returning from the NIH to Israel, I had to compete on research grant funding and have been lucky to be successful.

Q6 What are some of the most significant haematological or technological developments to have occurred during your professional career and how have they influenced your day-to-day work?

Amazingly, since I have started my career as a medical student, the outcome of childhood leukaemia has been transformed from an incurable disease to a cure of close to 90% of children with acute lymphoblastic leukaemia (ALL) and at least 70% of children with acute myeloid leukaemia. Now it is reasonable to set the goal to cure every child with cancer with less toxic, targeted, scientific-based therapies.

The most significant leap in the last few years has been the genomic revolution that enables us to administer more precise, personally adjusted medicine for treatment of both malignant and non-malignant disorders. The developments in fields such as genomic editing could lead to cure of many of the serious haematological disorders.

Q7 In your current lab, you are combining advanced genomics technologies with functional preclinical models to investigate haematological malignancies. Can you describe some of the difficulties you are experiencing in translating molecular findings into clinically relevant outcomes? How can this be improved?

Cancer is a complex disease driven by genomic instability and incredible versatility: one closes the door and it enters through the window. Ten years ago, we discovered a subtype of ALL characterised by acquired mutations activating the JAK–STAT pathway. We first discovered it in children with Down's syndrome and ALL. Later it has been discovered that this leukaemia characterises between 5–10% of children and adults without Down's syndrome and is associated with a poor prognosis. A trial with target therapy with ruxolitinib, a JAK inhibitor, is ongoing now in many hospitals of the Children Oncology Group (COG).

However, genomic analysis of diagnosis and relapse of these JAK driven leukaemia that we published a year ago demonstrate that JAK signalling at diagnosis is often replaced by RAS signalling at relapse. This observation is concerning. It illuminates a potential resistance mechanism to treatment with JAK inhibitors. Additional research is needed to study the interaction between these two signalling pathways and the proper way to target these high-risk leukaemias.

Q8 Looking forward to future EHA congresses, are there research topics that you believe are evolving rapidly and that will be increasingly popular points of discussion?

Immunotherapy, gene editing and gene therapy, interaction between cancer cells, and the microenvironment.

Q9 Finally, are there any points of advice you can offer to young haematologists experiencing and/or contributing to a congress for the first time?

As a physician I focus on children; they may be only 20% of the population but they are 100% of the future. In the EHA, we invest in young people because they are the future of haematology with our programme 'YoungEHA' directed at young haematologists, young scientists who chose the field of haematology, and young physicians who also want to pursue a career in science. It is combined from training programmes CRTH for clinical research and TRTH for basic research (partnering with the ASH); from special grants for early career scientists and physician-scientists; and from special programmes in the EHA congress. These are composed not only from special sessions during the congress, but also from a special pre-congress scientific meeting of PhD and postdoctoral fellows.

I have chosen haematology because this is the clinical field with the closest link between the lab and clinic. I was fascinated from seeing the disease under the microscope. This is the field that pushes the envelope. Problems and unmet needs of patients are taken to the laboratory where new discoveries are made that are quickly translated to the clinic and change patients' lives.

Doctor Marek Mraz, MSc, MD, PhD

Assoc. Prof. of Oncology
CEITEC MU and University Hospital Brno, Czech Republic
Member of the Young EHA Committee

Q1 How does YoungEHA promote the involvement of PhD students and young haematologists in the EHA congress and other important events?

YoungEHA organised a so-called 'Young EHA tract' during the EHA Annual congress, which was a series of sessions recommended to young haematologists/scientists. This year, we had several sessions specifically designed to attract and educate young researchers and clinicians. We had a 1-day pre-congress meeting (YoungEHA Research Meeting, Thursday 13th June, 8:45–18:00) that covered numerous interesting topics of basic and translational research in haematology and alternated young speakers and keynote lectures by top senior experts. During the congress, the YoungEHA session (Friday 14th June, 14:30–15:30) covered the different sides of haematology, from discovering a novel drug target to performing clinical trials, and also the processes at regulatory agencies. The second 'YoungEHA session' (Sat 15th June, 14:14–17:15) focussed on the future of haematology, personalised therapy, and the use of genomics. YoungEHA also helps to promote the Translational Research Training in Hematology (TRTH) and Clinical Research Training in Hematology (CRTH) classes, and I very much recommend that scientists and haematologists apply for these in the future. Finally, on Saturday night we threw an EHA Grooves party, which was open for everybody but it is definitely a great opportunity to have a good time with young peers.

Q2 Personally, what are your roles and responsibilities as a member of the committee, prior to and during the congress?

We rotate our duties each year, and in principle this involves organisation of the sessions that I have described above and giving input to other EHA committees regarding topics such as early-career membership, harmonisation of access to education in different countries, and the identification of future challenges in haematology such as integration of truly personalised medicine via genomic approaches. My responsibility this year was to design together with other members the structure of the YoungEHA sessions and select potential speakers. We also all help to promote the EHA congress, and prepare materials for the EHA press office. This year, several new members are joining the YoungEHA committee, and I will be rotating-off next year.

Q3 YoungEHA focusses on inspiring young haematologists and ensuring they reach their full potential; what type of support and opportunities does YoungEHA provide to help young haematologists progress in the field?

The short answer here would be to visit our website: https://ehaweb.org/youngeha/. This will provide useful information regarding all the interesting options for young haematologists and trainees. We have put lot of energy into developing this site in a clear and engaging way. I can mention several opportunities that should not be missed: i) the EHA provides research grants for young scientists and clinicians; ii) the TRTH and CRTH special training and mentoring programs are something that I cannot recommend highly enough; and iii) the Master Class online training platform.

Q4 Do you think there are the same opportunities now as there were when you were studying for your PhD or just starting your career in the field? How have things changed?

I think nowadays the science is even more interconnected and thus also more competitive than ever. I left the Czech Republic very early in my career, and I was very lucky that my supervisor and head of the department supported this. I was also lucky when I wanted to return back to Europe after my post-doc in the USA, since I was to be one of the first to receive the EHA Non-Clinical Research grant, which helped me to start my own group. I am not sure that I would have been able to do this without this support. I highly recommend that young researchers use all the training and grant options provided by EHA... They are all well organised and administratively non-demanding.

Nowadays, the mobility options for basic scientists are nearly unlimited, but there are some remaining limitations regarding the transferability of education and clinical training for physician/physician-scientists between different countries, for example between Europe and North America. At least within Europe, this should be addressed in the coming years, including the uncertainty around Brexit. I very much encourage young people to use the opportunity to find a great supervisor and mentor, something that can be done in their home country, but also anywhere in the world.

Q5 You work with young scientists in your lab: Do you instil the same ethos of YoungEHA in your own style of supervision? If so, how?

I have met some great people to emulate. These include Thomas J. Kipps, who I worked with for several years at the University of California, San Diego; Greg S. Nowakowski and Clive S. Zent from the Mayo Clinic, Minnesota; and Sarka Pospisilova and Jiri Mayer from our University Hospital in Brno, Czech Republic. I guess my style is a mixture of what I learned from these great people. I am trying to push each of my students to their maximal individual potential and acknowledge that each person has some specific talents and weaknesses that can be harnessed and worked on. However, sometimes I joke that the only thing that I can ever really teach them is to be curious and use proper positive and negative controls in their experiments. I also think that persistence and focussed work pays off.

Q6 Congratulations on winning the ERC grant from European Commission in 2018 for your research into chronic lymphocytic leukaemia (CLL) and B-cell lymphoma! How does this compare to other achievements in your career?

This is extremely important for my lab, and for developing our ideas and research field. We are interested in understanding microenvironmental interactions in chronic lymphocytic leukaemia (CLL) with a special emphasis on the role of non-coding RNA. We have recently showed in several studies that it appears that microRNA are regulating the B cell receptor (BCR) signalling pathway, and that this is deregulated in CLL/lymphomas. This grant allows me to support the lab, and I am looking for enthusiastic post-docs to join this project. It was also followed by multiple invitations to give lectures at conferences and institutes. It is important for the lab, but the only real achievement is the publications and research that my group produce: that is where all our work and passion goes.

"I am trying to push each of my students to their maximal individual potential and acknowledge that each person has some specific talents and weaknesses that can be harnessed and worked on."

Q7 Last year, whilst under your supervision, one of your colleagues won a Discovery award. How do you motivate and support young scientists around you to achieve their best?

Gabriela Pavlasova is my PhD student and she published two papers that defined the regulation and molecular function of CD20 in CLL cells. It is paradoxical that anti-CD20 monoclonal antibodies such as rituximab have been used for over 20 years, but the function of CD20 remains unclear. She showed that CLL cells, in the

context of immune niches, induce CD20 to boost BCR signalling, and rituximab interferes with this by eliminating cells with the highest levels of CD20 and thus more active BCR signalling. These observations also have implications for therapy, since she described that BCR inhibitor ibrutinib leads to down-modulation of CD20 by interfering with CXCR4 signalling. Practically, this means that ibrutinib is probably not suitable to combine with rituximab, and the Discovery award provided by Novartis acknowledged her for these discoveries.

Gabriela is very hard working, but it also took me about a year to find a project that fits her talents and natural inclinations. Not everything was easy, and I had to put some more time into discussions with her at the beginning of the project. Nowadays however she is very independent and runs multiple projects. It is a serious responsibility of the supervisor to put students on the right path, and it sounds easier than it is sometimes.

Q7 Have you observed any areas of research that particularly interest the younger generation of haematologists, or that appear to be an evolving topic of inquiry?

There are so many interesting things, and some of them are obvious in that many people see them, but many things remain unasked because researchers are blinded by the shiny and obvious problems.

My personal impression is that noncoding RNA will be a very fruitful and fascinating area of research, and a lot of young scientists envision this too. There must be a good reason for having >95% of our genome coding RNA that are not translated to proteins....

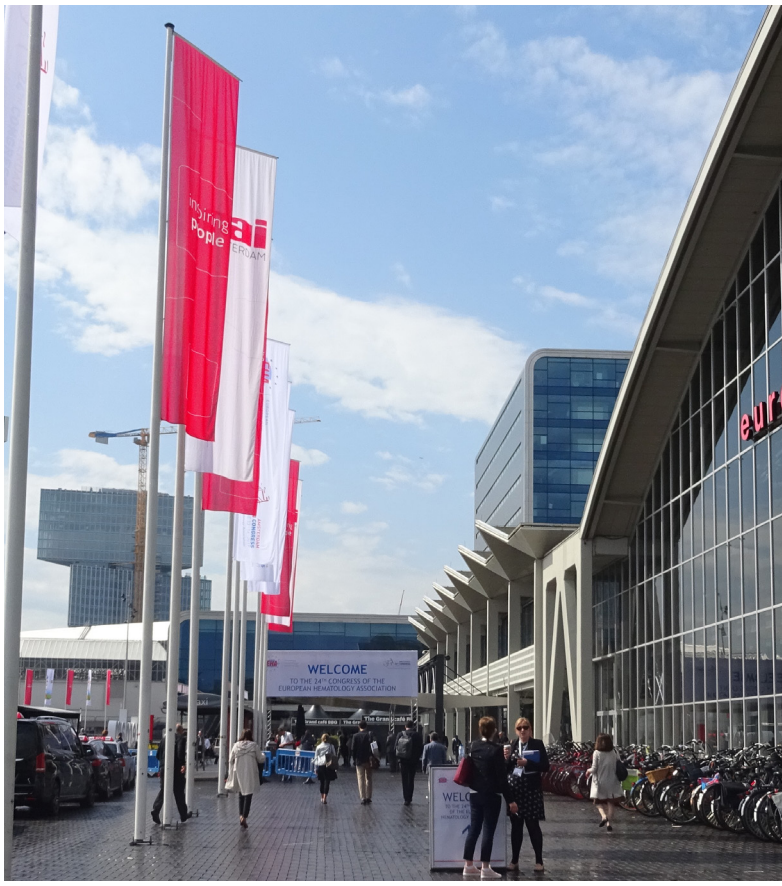
Young clinicians often also want to take up the challenge of performing a fully personalised therapy in patients. How to do this in a timely fashion, involving the sequencing of gene panels/genomes within days and the quick analysis of big data to make therapeutic decisions is difficult. There is a real need to figure this out. Do we need to combine targeted agents in a fully personalised fashion, and have clinical trials in which each patient receives a unique 'drug cocktail'?

Q8 How has the field of haematology changed since you started your career in research, and what developments are you most excited about for the future?

Everything has changed in last 15 years: we have next-generation sequencing techniques for analysing all layers of regulation; we have genome editing technology such as CRISPR/Cas; we have many newly discovered non-coding RNA; and we have BCR inhibitors developed for B cell leukaemia and lymphomas. I feel privileged to work in a time when we are finally starting to understand some problems in depth, and also witness many new drugs being approved for the benefit of patients.

Q9 Finally, do you have any advice to young haematologists who are starting their careers in the field?

The mentoring from supervisors that you receive and determining the scientific area you wish to specialise in is vitally important and is likely to affect your personal life too. Select your mentors carefully. Be ready to fail many times with your experiments (or unfortunately sometimes with your patients), but if you use good positive and negative controls you will always learn something for the next time.



Professor Barbara Bain

Imperial College, London, UK
Member of the EHA Online Case Unit

Q1 What is your favourite part of attending events, such as the EHA congress?

I must confess that my favourite part is meeting people that I have worked with or known in various contexts, complementary to the scientific part of the meeting.

Q2 As a member of the EHA online case unit, what does your work comprise?

I am one of four case editors. Between us we edit all cases that are to be presented at EHA tutorials, to make sure that the science is up to date and clearly presented, and also that the English is correct and the meaning is clear. This requires tact and active collaboration with the authors. Later, we each review all the cases that have been presented at EHA tutorials in the previous year and then meet to discuss which cases should be uploaded to the online EHA Campus. The cases are re-edited at this stage to make sure that they can stand alone when the author of the case is not there to answer questions. The online availability means that far more people can benefit than were able to attend the actual tutorial. I usually attend one tutorial a year, as do my colleagues. This lets us see how the cases work in practice and helps us to guide future authors. My most recent expedition was to Kazakhstan where the tutorial was part of the EHA's global outreach programme. The previous year I participated in a tutorial in Warsaw.

Q3 The practice of medicine is becoming increasingly multidisciplinary. How collaborative is modern haematology and with whom do you work most frequently?

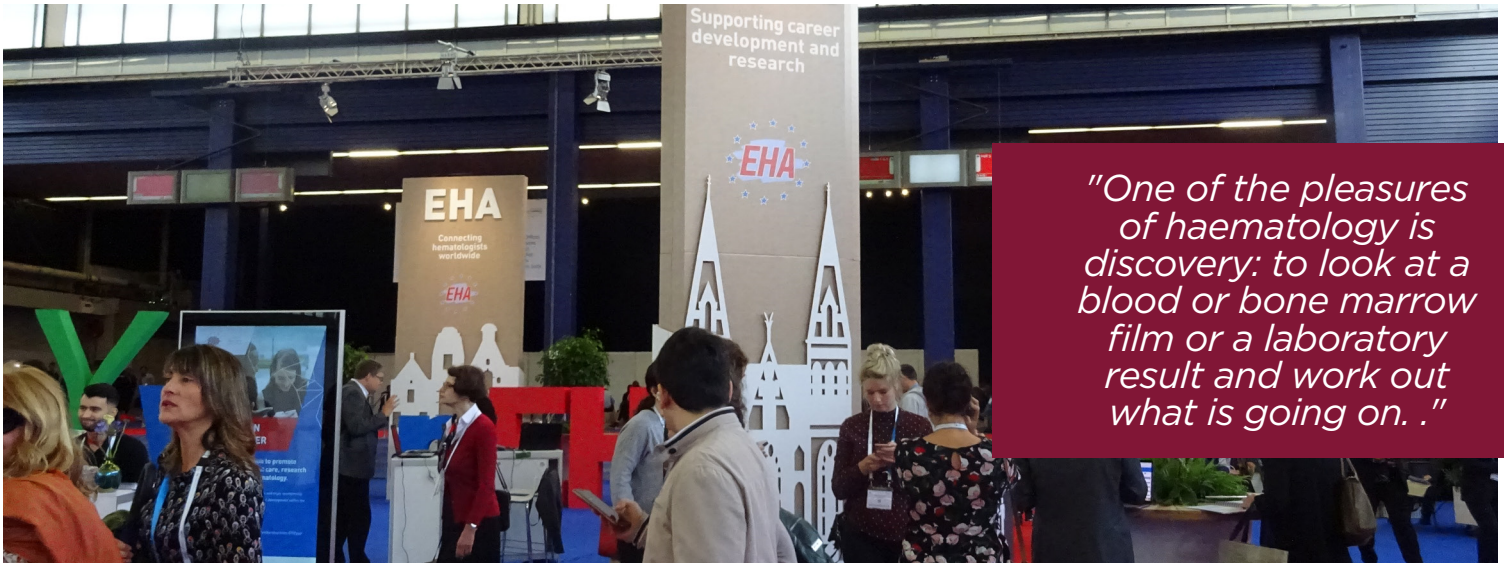
Haematology is very collaborative, but at the same time in some countries specialised tests are centralised so that there is a regrettable dissociation between the clinicians treating the patient and the laboratories that are performing specialised tests. I now work intermittently in the laboratory, collaborating with laboratory scientists, clinical staff, and trainees.

Q4 When did you first know that you had a passion for teaching?

This started as early as school. Some of my teachers were not very pleased when they found I was helping other students understand the lessons. Presumably they thought this reflected badly on them. I have continued to teach throughout my medical career. One of the pleasures of haematology is discovery: to look at a blood or bone marrow film or a laboratory result and work out what is going on. If this is done collaboratively with laboratory scientists or trainee haematologists, everyone learns from the experience. Formal lectures help, but sitting at the microscope with others can be more important.

Q5 You have spoken before of the importance of your mentors throughout your career. What do you remember most about their teachings and what qualities do you think make a good medical mentor?

The mentors that most influenced me were those who had both a keen interest in science and a deep understanding of the patient's experience. They dedicated hours each week, in the company of trainees, to diagnostic haematology and to discussing patient management. Like all good teachers they showed intellectual curiosity and continued to inspire others well past the usual retirement age.



"One of the pleasures of haematology is discovery: to look at a blood or bone marrow film or a laboratory result and work out what is going on. ."

Q6 The YoungEHA provides support to young researchers and clinicians throughout Europe. How important do you think groups dedicated to the next generation are for the future of this discipline?

Supporting the next generation is of great importance. The practice of haematology is not getting any easier with the increasing complexity of the subject and the enormous body of knowledge to be assimilated.

Q7 Burnout has recently been recognised as an occupational phenomenon by the World Health Organization and is of growing concern for medical practitioners throughout the world. How have you avoided burnout throughout your career and what advice would you have for aspiring physicians?

I think you need to accept focussing on just a small part of your discipline and work closely with others. A supportive secretary is pretty important. It is also important to have some interests outside medicine and some time when you can escape from the pressures of medical practice.

Q8 What is your opinion on social media as an education tool, especially for haematologists?

I am too old to have much interest in social media. It is all I can do to keep up with the daily flood of emails... No doubt it is important, but not for me.

Q9 What do you think were the main take-home messages from this year's EHA congress?

A large part of the congress was dedicated to understanding the nature of haematological neoplasms and assessing their optimal treatment. New and evolving treatment options will be in the forefront on the minds of many participants. These are continually being evaluated and then introduced into clinical practice. Participants will go back to their day-to-day work armed with the latest information.

Q10 Congratulations on being awarded a lifetime achievement by the British Society for Haematology in 2017 and an inaugural EHA Educational and Mentoring award in 2018! What will be the next milestone in your career as a haematologist?

I am not expecting any milestones, but I should like to keep learning. Teaching helps in this regard. *Docendo discimus*: by teaching, we learn. My advice to the next generation is to always have the courage to have an opinion on a diagnosis or optimal management. It does not matter if your initial opinion is wrong: what is important is to think about the possibilities for yourself and only then discuss it with others and learn from the experience. Of course, sometimes the only honest opinion is "I don't know what is going on here."