Milan Macek Snr

Personal Details	
Name	Milan Macek (Senior)
Dates	Born July 1932
Place of Birth	Czechoslovakia
Main work places	Prague
Principal field of work	Human and medical genetics

Interview	
Recorded interview made	Yes
Interviewer	Peter Harper
Date of Interview	16/10/2012
Edited transcript available	See Below

INTERVIEW WITH PROF MILAN MACEK (SENIOR), PRAGUE, 16 OCTOBER 2012

PH = Interviewer (Peter Harper)

MM = Milan Macek Snr

PH Today is Wednesday, 16th October 2012 and I'm speaking with Professor Milan Macek Sr. in Prague, Czech Republic. Milan, may I start by asking where and when were you born?

MM I was born in July 1932 in a small Moravian village called Hošťálková close to the border with Slovakia. My father was a forester, my mother was teaching at the local elementary school, which provided me with a good background to become interested in everything related to natural sciences. During my childhood and prior to the WWII (1932–1939) this part of Czechoslovakia was rather poor. This region also had a strong Protestant religious tradition, since it was settled by the so called Moravian Wallachians who have defended the freedom of their religion from the 17th century and fought against Catholic Habsburgs. Thus, Catholic families such as mine were in minority. Wallachians strongly defended what they believed in, irrespective of any personal profit, so this was a good example for me at the beginning of my life.

Then, after the German occupation in 1939 I recognised what fascism means. One of my best friends was a Jewish boy named Oscar Pollitzer. I still remember how in 1941, when going out of school, I have seen the entire family assembled on a small bridge and waiting for the bus to be taken to Auschwitz, nobody of them returned. Nazis took one of the excellent patriotic teachers from our village, a friend of our family, and again after several weeks we learned that he was executed.

From our and neighbouring small villages a lot of young people emigrated in a very complicated way to Britain. They fought in the air war, in the "Battle of Britain", some of them were trained there as paratroopers who later returned to this region as guerrillas, where they could perfectly hide in deep forests, Gestapo in revenge took their parents to concentration camps. I still remember that both parents of my school friends were hung because they supported them by providing them with food and shelter.

I was influenced very much by these sad historical events. The people of this region and my parents had been a strong example for me. These people fought for their religious or personal liberties, and despite being rather poor they were not afraid to give up everything, even their lives, for defeating the Nazis. Thus, as a small child I clearly recognised "bad things" and realised that it's necessary to try to do our best to fight against them.

In 1946 I witnessed the first post war free elections in which the Communist Party got more than 40% of the popular vote, since their main slogan was "More work for the benefit of the republic", that was badly destroyed by the war. At that time people enthusiastically wanted to build something better, something new, and this post-war euphoria influenced me, as well. I was happy that a lot of good things were done for poor people around us. As a child of state employees I felt uneasy having shoes, being well dressed, while my friends at elementary school told me that I am "rich boy" and they are "poor", had old clothes and went barefoot to school, even in cold November. Therefore, I sympathised with a lot of people who tried to create a more equitable society than before. I have to admit that given my childhood experience my heart has remained on the "left side".

Nevertheless, I did not enter to the Communist Party, even after early 1948, when they took over the federal government, because of the horrible political processes and since being a party member conveyed an unfair benefit for further professional careers of party members.

I appreciate that I had a great chance to study, at the reputable Masaryk gymnasium in the regional city - Vsetín. We received excellent education in history, literature, music, natural sciences and foreign languages, including Latin. After 1948 the government nationalised all forests and my father responsible for private forests moved to Prague, where I continued my college studies at the "Sladkovský gymnasium".

Due to my interest in natural sciences I decided to study Medicine at Charles University Prague. I virtually "fell in love" with medicine since I was convinced that if I would learn more, I could also be more beneficial to others. So that's the reason why I achieved top marks in all my medical examinations, not because I was some sort of a "talented student", but that I truly loved to learn the scientific basis of medicine, that is what is the underlying reason for a disease.

PH Before we go further: was there anyone in your family who had been in medicine or science, or were you the first?

MM Nobody. My mother was a teacher of biology, she was fond of botany and liked gardening. She even sterilised cocks herself by instruments borrowed from a friendly village doctor. My father was a forester, who liked to cultivate trees according to the latest recommendations. Thanks to them, I was attracted to biology and natural sciences.

During my medical studies at the Medical Faculty of Charles University in Prague I was fascinated by cellular pathogenesis of the disease", I had enjoyed pathology and physiology, including their clinical applications. I was inspired by the possibility of in vitro tissue cell cultivation, opened by pioneering work of Dr. Alexis Carrel and Prof. Emma Holečková in our country.

During my medical studies, at a defining moment of my professional life, I met a really great man, Prof. Josef Houštěk. He established an excellent organisation of paediatric care, founded truly multidisciplinary paediatric research in our country at the Institute of Child Development Research of Faculty of Paediatrics of Charles University and of University Hospital Motol in Prague. Once he guided me through his paediatric clinic, and when I had discussed with him my future medical specialisation he told me, "We need somebody who loves medicine and also likes to carry out research". Thus, I decided to switch my medical studies from the Faculty of General Medicine (originally called Faculty of Medicine until 1952) to the newly established Faculty of Paediatrics of Charles University in Prague (1953). At this faculty we of course studied medicine as elsewhere, but in addition to the standard medical curriculum it had an extra focus on paediatrics and developmental medicine. Its foundation was a reflection of high post-war neonatal and infant mortality which needed a new generation of specialists to tackle it. During my medical studies I even considered that I could later specialise in obstetrics since human prenatal development has been since then really fascinating to me.

PH At this point had you finished your medical qualification already? Was this after graduating?

MM I finished medical studies in 1957 with magna cum laude. As I said Prof. Houštěk, as the dean of the Faculty of Paediatrics inspired me to combine clinical practice with research. It has influenced my decision to start working at a paediatric department at an outstanding regional hospital in the Northern part of Bohemia located in Ústí nad Labem, virtually on the other side of the mountains that are close to Dresden. This hospital had excellent laboratories. Top clinical specialists chaired their main clinical departments. The department of paediatrics was chaired by my former teacher from the paediatric faculty Dr. Miroslav Mitera, who was specialized in haematology. This town had at that time heavy chemical industry. Therefore, during the foggy times a lot of children were suffering by severe acute respiratory diseases due to now unimaginable air pollution. Professionally I was very happy, because we had an excellent chance to learn a broad spectrum of acute paediatric diagnostics and therapy, including exsanguination transfusions in Rh incompatibility and chronic diseases, i.e. similarly as our colleagues in Prague. We had complete freedom to use new therapies

as e.g. hibernation in severe asphyxia, steroid therapy etc. When we did our best, we could then see direct outcomes of our approaches in “rescued” severely sick children. I also had the freedom to build a laboratory to test antibiotic sensitivity and thus to save children with meningitis, severe broncho-pulmonary diseases etc. by rapid optimal antibiotic therapy.

In the hospital dormitory I found a small room for testing of the role of penicillin on the tadpole transformation to frogs and their growth, to detect its presumed anabolic effect, based on the idea of my older colleague at our ward. I will never forget my colleagues who trained and inspired me to carry out medical research! However, I wanted to move forward and my dream was to join more advanced research teams in Prague, at paediatric clinics.

During the late fifties all medical faculties were undergoing “regeneration” of their staff. Older teachers were approaching their retirement age and that was the time when there appeared a chance to apply for a position in Prague to continue my postgraduate training. However, their official preferences were for young people who were also Communist Party members. Thus, a substantial part of my colleagues entered the Party in order to have a chance to work at such top facilities.

However, I still didn’t want to join the Party, just to be able to go to Prague. I was strongly convinced that I had to work for that position, be better, simply to deserve it mainly due to my competence. In 1960 following good recommendation from my “mother” hospital I applied for a vacant post in Prague, only to learn that by not being in the Party I was not accepted. I was so disillusioned! Nonetheless, I decided to remain at Ústí nad Labem where I had all freedom to carry out clinical research, and where I could still learn a lot.

All this happened at the period which some historians now call as ”Golden Era” of the sixties which culminated in 1968 by the “Prague Spring”. There had been a gradual thawing of dogmatism, and within the Party itself there were more and more people who recognised that it is necessary to move towards democratic socialism, with a “human face”. They aimed to change the Party “from the inside”, so to speak, by admitting honest people into its ranks to prevent such a counterproductive political discrimination. These people who were internal party reformers convinced me to join the Party and help them out with their goals. From the current perspective it may seem apologetic, but this period was full of sincere excitement and honest hopes for a better future.

In 1961 Prof. Houštěk had a chance to join a Czechoslovak delegation which travelled to the United States where he immediately realised how genetics will become important, particularly for paediatrics, and how this discipline will support his idea of “developmental medicine”. This view, which we now take for granted, was revolutionary at the time of Lysenkoism. I was very surprised when I received in the spring of 1961 from him a short letter in that I got a “job as a geneticist” at his Institute for Child Development Research of the Paediatric Faculty in Prague since August 1 1961, with an accompanying message “start to learn about it”. Simply, I was asked to establish a medical genetics department!

This appointment was not only surprising but also very challenging, since at that time I knew l very little about the subject. My wife Věra studied biology and botany at the Charles University Faculty of Pedagogy, at its Prague natural sciences branch. She initially helped me to pick up basic information on genetics (laughs). I am still amazed how previous political discrimination enabled me to participate in the developments of the fascinating field of medical genetics, and to become one of the founders of this specialty in our country (laughs).

PH Had you any thoughts before that about genetics? Or was it just really the chance

MM Naturally, I had been studying merely general biology in the first years of my medical studies. Therefore, as medical students we were not attracted to the potential impact of genetics on clinical medicine. Prof. Bohumil Sekla taught us already in the fifties about Mendelism-Morganism. His first and very talented assistant was Prof. Milan Hašek, who passionately fought against it. In his lectures

he promoted the idea that this “theory” cannot fully explain the “plastic genome development”. He also argued that human development is not only related to our “genes”, but also influenced by the environment. He was against the absolute or as we now say “deterministic” role of our genetic constitution. Currently, he is even in Western countries considered as one of the first promoters of epigenetics. But he was wrong, since he was “absolutistic” in his complete denial of Mendelism. I should mention that at that time the debate was very passionate “either / or”..., with Mendelism being viewed as “reactionary Western-”, while Lysenkoism was considered as being “progressive and Socialist ideology”. One should also not forget that the horrors of Nazi eugenics made a strong impact on our scientific community. After the punitive closure of our universities in 1940, because of the students protests, against the German occupation, the Nazis transformed the Prague Institute of Medical Biology of Prof. Sekla´s into the “Institut für Rassenhygiene”, which had been operating until the end of the war.

PH Medical studies and academic freedom

MM As I have already mentioned Communists came to power in 1948 and in 1949 I finished my college studies. In 1950 I started my medical studies and as I already said I became very interested in medical biology. This subject was presented by two excellent teachers, strongly opposing one another, and luckily we had the chance to see both views, and thus make up our minds ourselves. In this respect true academic freedom still had persisted at the Faculty of General Medicine. We appreciated that Prof. Sekla, who was not the member of the Party, proudly documented the scientific validity of Mendelism-Morganism and was opposed by the promotion of Lysenkoism by his colleague, a Party member, Prof. Hašek. Interestingly, both tolerated each other. Later Prof. Hašek left the Institute of Prof. Sekla, together with his assistants and founded the Biological Institute at the Czechoslovak Academy of Sciences elsewhere in Prague. There he independently discovered the basis of immunological tolerance. This discovery was awarded the Nobel Prize, but I just cannot now remember the name of the Australian scientist, who received it ...

PH Macfarlane Burnet?

MM Yes, yes. The same discovery, but less than approx. 14 days difference of publication date caused that Milan Hašek missed the chance to get the Nobel Prize!

Prof. Hašek realised that he had made a great mistake in completely opposing Mendelism-Morganism. I will never forget a meeting of the Academy of Sciences in the Autumn of 1961 in Prague. The representatives of the Czechoslovak Academy of Sciences denounced officially Lysenkoism as an ideological deformation of science, with the deleterious political impact on the scientific development in genetics, including its scientific proponents. I was deeply impressed that Prof. Hašek had the courage to openly declare to the audience that he is sincerely sorry for being wrong in opposing prof. Sekla´s defence of Mendelism, and asked him publically for an excuse. Prof. Sekla with the grace of a British gentleman sincerely accepted his apology!

His apology in 1961 heralded the “official end” of Lysenkoism which was later declared as obsolete in 1965 at Brno World genetic congress. This important meeting was held to commemorate the 100th anniversary of the publication of Gregor Mendel´s papers based on experiments carried out at a small garden in front of the Augustinian monastery in this city.

I also had recognised how it’s important in science not to only be “happy” if you are successful, but also to be able to admit that we are after all humans and that it’s natural that we err. ..

Within 1961-1967 Prof. Hašek supported further development of medical genetics. He developed at the Czechoslovak Academy of Sciences an excellent experimental immunogenetic laboratory and his own school with important scientific contributions. He was the generation of Prof. John H. Edwards and the famous English embryologist, Prof. Anne McLaren, who had appreciated his scientific achievements.

I am grateful that Prof. Hašek was my postgraduate scientific mentor when I became in 1961 the first "PhD student" in medical genetics in Czechoslovakia. He included in his team other talented graduates of the Faculty of Paediatrics. Thanks to the initiative of Prof. Houštěk these were Dr. Eva Seemanová (clinical genetics) and Dr. Mária Kučerová (cytogenetics) who became first official postgraduate students in medical genetics. Prof. Houštěk realised how important is to prepare the education of different specialists for complex medical genetic services.

Prof. Hašek´s Institute designed a grant for the population genetic study of persisting isolated populations in Slovakian mountainous regions to ascertain the genetic load and impact of endogamy, and incest, based on the incidence of inherited disease and malformations. Dr. Seemanová and Dr. M. Matoušek, an excellent mathematical population geneticist, were responsible for the evaluation of this study results. This pioneering study and its outcomes supported further scientific development of Dr. Seemanová in genetic counselling, genetic dysmorphology and in the detection of new syndromes. Dr. Kučerová later built a successful second department of clinical genetics in Prague at the Thomayer Hospital, contributed to the implementation of chromosomal banding methods and developed a nation-wide system for postgraduate education in medical genetics for doctors, nurses and laboratory personnel.

Prof. Sekla chaired the Institute of Medical Biology (established in 1911) at the Albertov district of Prague until his retirement. In the sixties he was engaged as a member of the scientific board of the Ministry of Health and prepared with Assoc. Prof. Miloš Černy initial grant support scheme for medical genetic projects.

Prof. Sekla awarded me and my co-workers with the first Scientific Award of the Ministry of Health in medical genetics in 1968, appreciating results of my PhD thesis on cytogenetic and biochemical studies in short- and long term cultivated human cells.

Assoc. Prof. Černý later developed the Department of medical genetics within the Institute of Prof. Sekla which was among the first to be included into the national health care genetic services. His postgraduate student Dr. Jan Kapras introduced preconception prevention of neural tube defects by the application of folic acid since the seventies.

Prof. Sekla and Prof. Charvát, representing clinical research in internal medicine, as members of the Scientific Board of the Ministry of the Health facilitated the establishment of the Society of Medical Genetics of the Czech Medical Society of Jan Evangelista Purkyně in 1967. Foundation of the federal medical genetics society also meant that this specialty got officially recognised alongside of other medical disciplines in our country.

Prof. Charvát promoted clinical genetics studies the IIIrd Clinic of Internal Medicine of the Faculty of General Medicine of Charles University Prague chaired by him. There Dr. Radovan Chrz and Dr. Jiří Neuwirt established at that time an excellent cytogenetic laboratory, where Prof. Dipl. Ing. Kyra Michalová concentrated on oncocytogenetics of hematologic malignancies. Dr. Josef Šobra also developed a laboratory for the study of hereditary dyslipidemias at this clinic.

Another important historical event was the establishment of the Cytogenetic Section of Czechoslovak Biological Society by Assoc. Prof. Dušan Soudek from the Institute of Paediatrics in Brno, by myself and and Dr. František Soukup from Prof. Sekla´s Institute in Prague in 1963. Since then this section has been organising regular cytogenetic meetings, commonly with cytogeneticists from all COMECON and Western European countries, especially from Germany, Italy France, United Kingdom, Sweden, Denmark and the former Yugoslavia We were also happy to build bridges between Western and COMECON countries, between divided west and east part of Germany thanks to these conferences. It opened broad exchange of information, technologies and made possible to start international collaborations even before 1970. These activities continued until 1989, despite the unfortunate Iron Curtain blockade.

The first Department of Medical Genetics in Czechoslovakia was established by Prof. Houštěk at Institute for the Child Development Research on August 1, 1961. Following the discovery of the cytogenetic basis of Trisomy 21 and of the other most frequent chromosomal aneuploidies I decided to learn cytogenetic methods. I started cytogenetic examinations by direct preparation of bone marrow cells by a "squash method" which I learned from Dr. Černý. I had modified this method by short term overnight cultivation, which rendered more mitoses with significantly better quality of chromosomes using an air drying method for chromosome spreading. Thanks to it I was able to present already in November 1961 at a Paediatric meeting the first cytogenetic detection two Turner syndrome cases.

I need to say that it was fascinating to see living cells in vitro under the microscope and to learn how to cultivate them, and to see the chromosomes. At the beginning I did not have a laboratory, nor the possibility to work with the living cells at our Department. Luckily, I had a great chance to meet an inspiring biologist Dr. Jiří Michl who had been working at the Institute of Sera and Vaccines in Prague, and who was in charge of its tissue culture laboratories. He allowed me to work over there and his co-worker Dr. Dagmar Řezáčová trained me cell cultivation. Dr. Michl invented a special tissue culture medium "EPL"- a combination of media Eagle, Parker, enriched with lactalbuminhydrolyzate and alfa-2 macroglobulin. This allowed successful cell growth without any serum supplementation, and got published in Exp Cell Research in 1965.

His laboratory has been preparing culture media for cell lines for virology and polio vaccine production. I had free access to everything, but only after his laboratory finished their daily programme. I was then working like a night owl (laughs). I could use their cultivation hoods for experimental human cell cultivation for cytogenetic, biochemical and biological studies. In the beginning I used Michl´s medium for short term culture of bone marrow cells. This approach enabled good growth of cells which attained "fibroblast like" morphology. Afterwards in 1961 I introduced for the first time in our country serial long term culture derivations of embryonic cells from different tissues and operation biopsies, together with the successful cryopreservation of derived diploid human cells on dry ice. This method was patented for production of diploid cell strains in virology studies.

I studied human cells till the end of their life in vitro, evaluated their growth characteristics, assessed incidence of chromosomal aberrations and used biochemical investigations for study of collagen synthesis. I had realised, that the basic idea of Prof. Houštěk that normal and pathological development in children could only be understood by their long term, complex, follow up. I confirmed that this can be tested also in vitro by long term parallel cultivation of human cells derived from normal and affected donors. I disclosed that the speed of cell outgrowth from tissue fragments is decreasing with the age of the tissue donor, which was confirmed by Dr. Holečková. Moreover, I revealed that long-term cultivation and cell senescence in vitro are associated with increasing prevalence of minority clones with chromosomal aberrations and heteroploidy, that is highest in the final degenerative phase of human diploid strains during their in vitro development.

Thanks to the cooperation with excellent biochemical team of Dr. Miloš Chvapil and Dr. Josef Hurych we documented collagen synthesis in human diploid cells in vitro in studied fibroblastoid cells. Senescence of the cells was characterized by the decrease of collagen solubility that was produced by them. These biochemical studies substantiated my hypothesis that Marfan syndrome could be associated with a disorder of collagen synthesis. We revealed, comparing controls a disorder of collagen maturation of cultivated Marfan syndrome fibroblasts, published in Humangenetik in 1966. We had also proved that we could derive fibroblast cultures for up to 3 days following post mortem biopsies for further genetic examinations.

The achievement which I value most from my early research was the stem cell detection in derived embryonic cultures with the differentiation of CNS cells not only from the brain-, spinal cord-, but

also from embryonic retinal- and suprarenal gland tissues. As far as I know, this is the first observation of persistent stem cell cultures generated in vitro. As scientific beginner, unfortunately, I did not publish this observation. Therefore, I can only show it to you in my PhD thesis book on microphotographs.

In 1962 I started to used short term cultures of peripheral blood using own preparation of phytohemaglutinin from different sorts of beans before its commercial version was available for cytogenetic clinical examinations. Experience with different types of long and short term cultivation of human cells were used for the detection of chromosomal aberrations in vivo, post mortem, and also for examination of childhood leukaemia, tumours, including chorioepithelioma, testing of chromosomal mutagenesis after X ray irradiation or even LSD misuse. In summary, I created a small laboratory in the cellar under the old paediatric clinics at Prague Karlov district, with my first co-workers we also shared this "cytogenetic cellar" with rats, but not those used in laboratories....in free time we even shot them with air guns (laughs).

PH Could you travel abroad, get for instance a stipend in medical genetics?

MM Yes, due to the gradual melting of the political climate I was able to travel out of the country during at the height of the Prague Spring. Thus, from 1968 to 1970 I could utilise fellowship offer from the Baylor University College of Medicine in Houston, right after the defence of my PhD. This was due to my other unique life chance to cooperate with internationally recognised virologist Prof. Vladimír Vonka during my work at the Institute for Sera and Vaccines. He prepared together with Dr. Dimitri Slonim a vaccine against poliomyelitis, he started first studies with oncogenic SV40 virus, later with papilloma viruses in cervical cancer. At that time Prof. Vonka closely collaborated with Prof. Joseph L. Melnick, founder of modern virology, from the Department of Virology and Epidemiology at Baylor in the studies of EB virus-related oncogenicity. He recommended me to Prof. Melnick that I could perform cytogenetic studies in lymphoblastoid cell lines derived from controls, EBV infected individuals and Burkitt lymphoma patients by his wife, Prof. Mathilda Benyesh-Melnick, including their excellent team.

My fellowship goal was cytogenetic comparison of EBV positive and negative lines, the study of their clonal evolution during the long term cultivation in vitro, in order to find possible specific chromosomal aberrations, at this time by classical karyotyping and to detect possible structural chromosome aberrations. This study disclosed selective growth advantage of cells with certain types of aneuploidies, especially with chromosome 8 trisomy, typical for leukaemias and the development of abnormal chromosomal clones found in human tumours, even in cultures derived from normal controls, indicating possible multiple clonal kryptomosaicism in apparently healthy humans. Published papers from my stipend were later included in a special monograph in the USA.

In Houston I had a unique chance to work and learn in top scientific community, not isolated as at the beginning of my career. I met the famous scientist, Prof. Tao-Chiuh Hsu, who reminded me in his lecture that one needs to be attentive to unexpected experimental observations and follow up on them. His technician by error washed cells in hypotonic instead of isotonic solution. Prof. Hsu did not throw them away but rather looked what could have happened and found out that he could see nice chromosomes (laughs).

I left for US in July 1968 and when a month later Soviets and its allies brutally crushed the Prague Spring movement by their invasion of our country they also destroyed our dream of creating democratic socialism with a "human face". I was deeply moved by the general show of solidarity from my Houston colleagues and people whom I had not known before, all of whom valued the struggle of our people for a better and more democratic system. Luckily, my wife and son Milan Jr. were still able to join me in early September 1968.

I considered Texas as my second homeland. There I had met not only helpful and friendly American families, but also a lot of Moravian immigrants originating from villages nearby my birthplace. They had cultivated their language, maintained traditional customs, baked traditional bread and "kolaches", special pancakes, that were very popular in Texas. Czech was the fourth most common language and I could even listen to Czech songs on radio in my car (laughs). In Houston October 28, the Czechoslovak Independence Day, was considered as a memorable day to honour contribution of our compatriots to the excellence of Texan agriculture.

Nonetheless, after two years our stipend had expired. After thorough consideration, myself and my friend Prof. Vonka decided to return home, despite the fact that we both were offered a good position at the Institute of Prof. Melnick, together with generous arrangements for our wives and children. We felt, that we have to return back to our country, humiliated by the Soviet invasion, transfer our research experience and not abandon our parents. It was a very difficult decision, but with hindsight we do not regret it.

Right after my return from the USA I started again with experimental human cell cultivation. I tried to develop lymphoblastoid cell cultures from foetal peripheral blood of aborted foetuses. I did not succeed to derive lymphoblastoid cell cultures, but fibroblast-like stem cells producing collagen in vitro, as proven by electron microscopy studies conducted by Prof. Karel Smetana and by biochemical examination carried out by Dr. Hurych. These results were published in a 1973 Academic Press monograph.

At the same time I have been systematically testing methods of the cultivation of amniotic fluid cells in order to prepare a solid basis for prenatal diagnosis. In derived long term cultivated diploid strains from amniotic fluid cells with predominantly fibroblast-like morphology. Surprisingly, we again revealed synthesis of collagen, published 1973 in a letter to Nature. Both studies brought the first evidence of the presence of embryonic mesenchymal stem cells in foetal peripheral blood and long term cultivated amniocytes.

PH **May I take you back a little bit now and, thinking of your publications, I looked at a list on the computer. Am I right that the first of your publications was on Turner's syndrome and chromosomes, cell culture?**

MM Yes, in the already mentioned Turner's syndrome publication I tried to point out clinical impact of cytogenetics for the better understanding of chromosomal pathogenesis of severe disorders of development, for their early prevention, diagnosis and treatment. In my other early publications I had summarized my experience with human diploid cell strain derivation, their post mortem cultivation, possibility of their use in cytogenetic analysis of leukemias or other tumours, detection of exogeneous mutagens, including viruses, chemical mutagens and monogenic diseases as documented in the Marfan syndrome paper and ageing at the cellular level. I was fascinated by the possibility of embryonic cells differentiation in vitro as possible perspective for their use in the treatment of severe diseases and traumatic lesions of CNS, and other diseases. All these studies are documented in my "voluminous" PhD thesis, here in front of you on the table (laughs).

PH **I saw in the list that I looked at that you had a paper, I think in 1971, on amniotic cell culture and prenatal diagnosis. Was this the beginning of prenatal diagnosis in the whole of Czechoslovakia?**

MM Yes, it was a family with previous delivery of the child with a D/G chromosome translocation form of Down syndrome who delivered an unaffected child following prenatal diagnosis already in 1970. It was referred to us from another "pioneer of clinical cytogenetics" Dr. Chrz, whom I had already mentioned. We were so happy that we could confirm an unaffected female foetus, with a balanced translocation. This family opted for pregnancy only since we could offer them prenatal diagnosis! In the first 2 weeks the mother even couldn't believe that her baby Markéta will be healthy. Now there is already the second generation of "this first baby" which underwent prenatal diagnosis in our

country. This family has been in close contact with us since that time. This was the first prenatal diagnosis performed not only in our country, but also in continental Europe! Amniocentesis was performed at the Clinic of Obstetrics and Gynaecology of the Faculty of Paediatrics by prof. Dr. Vladimír Fuchs

Afterwards, we provided prenatal diagnosis for Dr. Antonín Zwinger from the Institute for the Care of Mother and Child in Prague. The cytogenetic analysis was guaranteed by one of our top cytogeneticists Dr. Ivan Šubrt. Furthermore, we cooperated in prenatal diagnosis with Clinic of Obstetrics and Gynaecology of Faculty of General Medicine with Prof. Zdeněk Hájek and Dr. Eduard Kulovaný. Together with them we also introduced first CVS prenatal diagnosis in our country in collaboration with Prof. Bruno Brambati from Milano.

The prenatal diagnosis programme and its successful development in other genetic departments significantly contributed to the recognition of medical genetics as one of the important disciplines of medical prevention and for the implementation of the government public health programme of "integrated care" for the mother and child.

PH I saw that coming a little bit later you started to publish papers on inborn metabolic errors and storage diseases?

MM Yes, it was another line of my professional interest, since I am originally a paediatrician who treated these children in Ústí nad Labem. Due to the fact, that we could provide reliable cell cultures from different tissues, skin biopsies, from amniotic fluid cells, tissues from aborted embryos/foetuses, autopsies together with their freezing for further examination in genetic risk families after the elaboration of new methods for the biochemical detection of metabolic disorders at the cellular level. We provided this prenatal service for all genetic- and/or clinical departments in the former Czechoslovakia. Since then and in fact until today we guarantee very good biochemical genetics at the Institute of Inborn Errors of Metabolism in Prague Karlov Paediatrics Clinics, that was founded by Prof. Josef Hyánek, who was the pioneer of their diagnosis, prevention and treatment in our country. I would also like to point out excellent cooperation in prenatal and postnatal diagnosis of lysosomal storage diseases later with Prof. Milan Elleder at this Institute.

In amniotic fluid we studied levels of alpha-1-fetoprotein, alpha-1 antitrypsin, albumin, including enzyme activities (cholinesterase, alpha amylase, alkaline phosphatase) for improving prenatal diagnosis of neural tube defects, chromosomal aberrations or levels of steroid hormones for prenatal detection of disorders of sex development (Dipl. Ing. Petr Dvořák, Dr. Jana Šulcová).

I should also mention excellent cooperation with the crews of our national airlines that kindly transported in the plane cockpit living cell cultures to our cooperating Western colleagues for biochemical diagnoses. Intriguingly, in seventies and eighties despite travel limitations to Western Europe the government was not hesitating to put "hard currency" into funding of patient travel expenses for prenatal diagnosis of haemophilia or Duchenne muscular dystrophy, which required foetal blood sampling for rapid detection of these diseases in male foetuses at the department of prof. Kypros Nicolaides in London. His support for the development of prenatal diagnosis in our country is highly appreciated by all of us.

Now in retrospect I am still amazed that we could directly ask for "urgent funding in hard currency" at the Ministry of Health or even when their funds for this purpose were exhausted receive this funding in Ministry of Finances. Having assured funding I could directly ask the Ministry of Foreign Affairs for assistance with visas and transport of women by Czechoslovak airlines to London. Our embassy arranged their accommodation in diplomatic housing (laughs), transport to Prof. Nicolaides´ department and back after the procedure. Unaffected boys were diagnosed and not aborted, everything was free of charge.

Nevertheless, somebody reported to the Central Committee of the Communist Party that I am misusing the state support and that I am “making money” by such demanding services from the patients. In the end the resulting audit disclosed that one of such pregnant ladies was a milkmaid at a cooperative farm, while the other one was employed for postwoman and that two unaffected boys were delivered, without my direct personal contact with them. In the end this case promoted genetic prevention by prenatal diagnosis at the highest government and Party hierarchy levels (laughs).

My scientific work and of my co-workers, contributing to the implementation of biochemical prenatal diagnosis were appreciated by the second Award of Ministry of Health.

PH Can I ask you a little bit how medical genetics developed in what was in that time Czechoslovakia? Now was Prague the first place to develop medical genetics or it has also developed in Brno?

MM As part of care for “hereditary health“ Prof. Sekla was the first to initiate genetic counselling prior to WWII. His colleague Prof. Otakar Hněvkovský from the Clinic of paediatric orthopaedics collaborated with him in the study of heredity of congenital hip dislocation. Prof. Hyánek introduced biochemical genetics for phenylketonuria in the late fifties. Systematic development and organisation of first cytogenetic laboratories and genetic departments occurred at all 3 medical faculties of Charles University in Prague. In our Institute, as has been already discussed, was carried out under the guidance of the Genetic institute of Czechoslovak Academy of Sciences lead by Prof. Hašek.

First textbook on medical genetics, written by Assoc. Prof. Černý from Prof. Sekla´s Institute was published in 1967, Introduction to Clinical Genetics was edited by Dr. Kučerová together with 12 co-authors in 1978. I contributed with genetic chapters into textbooks of pediatrics and stomatology for medical students and in Proceedings of Pediatrics.

Departments of Medical Genetics had been gradually developed within the sixties at all medical faculties of Charles University in Prague, Plzeň (Dr. František Lošan), Hradec Králové (Dr. Jan Žižka), in Brno as part of the Institute for Paediatric Research chaired by Prof. Zdeněk Brunecký, later in Olomouc (Dr. Jiří Šantavý), in the eighties regional departments of medical genetics in České Budějovice (Dr. Karel Čutka) and Moravská Ostrava (Dr. Melánie Ševčíková, Dr. Jan Všetička) were finally established. This network now evenly covers the entire country, thanks to the Conception of medical genetics of the Ministry of Health.

Prof. Brunecký, a paediatrician, in parallel with Prof. Houštěk developed top department of medical genetics in the early sixties at his Brno Institute. He estimated the incidence of cystic fibrosis in the Czech population. Interestingly, both Prof. Houštěk and Prof. Brunecký used cystic fibrosis as a model “Mendelian” disease in children. Our colleagues in Brno also developed an outstanding cytogenetic department chaired by Assoc. Prof. Dušan Soudek, to him I transferred our experience with human tissue cell cultures. Dr. Milan Vrba from Brno was the first Czech colleague who was awarded with a cytogenetic fellowship to Germany already in 1964. This institute developed at high level biochemical genetics (Drs. Jan Kamarýt and Antonín Mrskoš). Clinical genetics and syndromology was developed there by Dr. Renata Laxová. In Olomouc Dr. Dagmar Kalousek, cytogeneticist, who later became famous for detecting confined placental mosaicism.

One should also not forget Prof. Vítězslav Orel at the Mendel Museum who has been studying the professional life of this genius of science, and published several international monographs on this topic.

Unfortunately, after the Soviet invasion in 1968 Dr. Kalousek and Assoc. Prof. Soudek emigrated to Canada, as well as, Dr. Laxová to the USA, and there all of them achieved international recognition in their fields.

In 1965 our colleagues from Brno hosted the Gregor Mendel´s centenary conference. The colleagues from the Soviet Union finally refused Lysenkoism, German scientists denounced the misuse of genetics by the Nazis. We also learned how Russian scientists conducted excellent research in the thirties (e.g. by Prof. Nicolai Vavilov), which sadly ended in 1940 by an official denial of Mendelism by the Stalinist regime and when Vavilov was sent to Siberia, where he later died.

The Brno meeting was a crucial event which started our international collaborations, both with former COMECON and Western European countries. The Brno group contributed to international cooperation by active organisation of cytogenetics conferences, rotating around other genetic departments, each in various towns of our Czech and Slovak countries.

I am happy also to mention, that we had an excellent cooperation with the departments of medical genetic in Slovakia since the beginning of the sixties, represented by Prof. Viliam Izakovič in Bratislava in the area of medical cytogenetics, Prof. Štefan Sršeň and his wife Klára in biochemical and clinical genetics (Martin), Prof. Vladimír Ferák in population and molecular genetics in Bratislava. They all published several wonderful textbooks of medical and population genetics, which have been used until the recent decade by our medical students and in postgraduate education.

Together with Prof. Izakovič we prepared in 1980 a Scientific prognosis of the healthy development of new generations until year 2000 for the Academy of Sciences Subsequently in 1980, for the Ministry of Health of Czech Republic I elaborated a document for prognostic study of medical sciences development till year 2000, published in a special monograph. This document included medical genetics as integral part of medical research, health and social care, in “prenatal and postnatal development of new generations”. This strategy was verified and remained valid for planned scientific grant calls, with my update in 2007, until 2015.

PH Were you at the Brno 1965 meeting?

MM Indeed, I was there, it was a great event, and I presented my first lecture on an international congress, where we reported the disorder of collagen maturation in Marfan syndrome, which later got published in Humangenetik by Prof. Friedrich Vogel, who was present at this meeting as well. Since this time we have started to develop our international collaborations, including also excellent colleagues from the Soviet Union, from the Medical Genetics Institute of Prof. Nikolai P. Bochkov in Moscow, including other laboratories, whom had not known previously. There I also met Dr. Jan Žižka, with whom I studied medicine. Dr. Žižka later founded the Department of Medical Genetics in Hradec Králové with successful clinical genetics and cytogenetics units led by Dr. Petr Balíček. He later published a pioneering Czech monograph “Diagnostics of syndromes and malformations”, containing a unique collection of his own photographic documentation of syndromes encountered during his professional life.

PH May I ask in where?

MM Hradec Králové is regional centre of Eastern Bohemia. It also has a separate medical faculty of Charles University Prague, which at that time was also involved in the training of military doctors.

Also, we must not forget the role of the Society of Medical Genetics of the Czechoslovak Medical Society of Jan Evangelista Purkyně in the development of our field. This society covered entire Czech and Slovak parts of the former federation and was an official professional organisation, recognised by the government with the right to organize national, international congresses, education and scientific meetings and to influence policy decisions of the federal Ministries of Health (Czech and Slovak) concerning implementation of medical genetics in health care.

As its Scientific Secretary I was authorized in 1978 to prepare document of the “conception” of medical genetics implementation in health care. In fact, the first draft of this comprehensive medical

genetics policy was prepared by Dr. Černý at the end of the sixties that suggested the role of medical genetics, but was not legalized and not introduced to the clinical practice.

After 2 years of intensive discussions with the responsible persons at the Ministry and thanks to the support of Prof. Houštěk from the Scientific Board of the Ministry, the conception document was approved by Minister and published in official Bulletin with legal validity and obligatory fulfilment in all regions.

This document required obligatory organisation and establishment of departments of medical genetics in all administrative regions of the country, with outpatient wards to genetic counselling, cytogenetic laboratories with cell culture facilities, specialised laboratories for biochemical genetics, immunogenetics, prenatal genetic diagnosis with sufficient number of clinical and laboratory rooms, laboratory personnel, nurses, medical doctors and specialists with university education, obligatory laboratory equipment and financial support . In this document, we stipulated conditions for pregraduate- and postgraduate genetic training in medical genetics both for doctors, nurses and laboratory experts. Grant support of medical genetic research was also assured. This conception was distributed before official approval to all departments of medical genetics for critical evaluation. I consider that we had a first comprehensive official policy of medical genetics in health care in the world!

The era of “begging” for space, money and personal ended, because the official policy had to be fulfilled (laughs). For me it was gratifying to witness that Milan Jr. arranged recognition of medical genetics at the European level in 2011 as the acting President of the European Society of Human Genetics, which had reflected upon what we had achieved already in 1980.

Thanks to this official “Conception” I could develop together with my close collaborators Prof. Seemanová and Prof. Goetz, our former postgraduate PhD students from the original small genetic “cellar” department, the Centre of Medical Genetics as an integrated facility at the newly built University Hospital Motol and Paediatric faculty from the mid-seventies. We offered medical genetic health care research, including pregraduate and postgraduate education. The same was true for all other regional departments.

Although the Society of Medical Genetics had in the eighties only approx. 150 members compared to other larger medical societies, it had organised the highest number of workshops where we could invite top foreign geneticists. That was my duty as its Scientific Secretary. My last goal in this function was to organize the World congress on Early Foetal Diagnosis with my co-workers in 1990, which was considered as one of the most prominent genetic congresses of this year. With Prof. Malcolm Ferguson-Smith I edited monographic proceedings of all presentations. It again extended our international collaboration that enabled also the possibility of training of our young colleagues at top European genetic departments.

Thanks to Prof. Houštěk we had already since the eighties inter-university exchanges with genetic institutes at universities in Uppsala (Prof. Karl Henrik Gustavson, Prof. Goran Annerén), in Rotterdam, Hamburg and Essen with colleagues involved in biochemical genetics as I mentioned before, at KU Leuven with Prof. Jean-Jacques Cassiman and his co-workers.

Excellent cooperation was also with the Genetic Institute of Free University in Berlin chaired by Prof. Karl Sperling with whom we have cooperated in cytogenetics, and later studied together, among other topics, the mutagenic effects of the Chernobyl accident within a European research project Copernicus II. His co-workers, Prof. Jörg Schmidtke and Dr. André Reis trained our postgraduate student Dr. Milan Macek Jr. and thus supported implementation of molecular genetic methods for cystic fibrosis research, diagnosis and prenatal prevention.

Within COMECON countries we had wonderful collaboration with top genetic representatives from the former German Democratic Republic from universities in Berlin, Jena, Halle, Magdeburg and

Rostock, where medical genetics has also been rapidly developing since the sixties. I remember Dr. Brigitte Mauerberger. I prepared for her monograph on tissue cultures chapter on human cell cultivation. Prof. Regina Witkowski from Charité Berlin closely cooperated with Prof. Seemanová in dysmorphology. She also had fruitful cooperation in clinical genetic counselling with the Moscow Institute of Medical Genetics (Prof. Svetlana Kozlova), Prof. Goetz worked together Dr. Nikolai P. Kuleshov environmental chromosomal mutagenesis. We also highly appreciated research with Prof. Yuri Yurov and Prof. Svetlana Vorsanova at the Moscow Institute of Psychiatry and Paediatrics. We prepared together FISH for sperm analysis and successfully participated in the EU project Copernicus I (coordinated by Prof. Yurov) and Copernicus II projects, which was coordinated by me.

The successful development of medical genetics also resulted in the foundation of the Society for the Study of Environmental Mutagenesis by Prof. Radim Šrám in the seventies.

Importantly, COMECON funded international project to support the "healthy development of new generations". Thanks to Prof. Houštěk we were strongly represented in medical genetics. I was authorized to coordinate this genetic research in our country. This funding significantly enriched our genetic departments, involved I this project, with expensive instrumentation.

Professors Houštěk, Sekla and Charvát included in the ministry plan of medical research of the Ministry of Health also medical genetic research, coordinated first by Assoc. Prof. Černý already before the end of the sixties. Afterwards in early seventies I coordinated it with Dr. František Soukup. This research plan was concentrated on the problems of genetic counselling and clinical genetic diagnosis.

PH **Thank you!**

MM So you can now see how medical genetics has been developing in this country until the end of the eighties

PH **Yes. Can you tell me a little about how the Communist regime has affected medical genetics in this country? Because I know from what you and others have said that the Communist years had both good and bad aspects.**

MM Yes.

PH **So what has changed both for the good and for the bad since the change in regime?**

I will try to summarise it from my point of view and from the perspective of my work at the Department of Medical Genetics at the Institute of Child Development Research, because the proportion of good and bad aspects was different at various places and institutions, and had been highly dependent on the moral and scientific qualities of the people involved.

Lysenkoism per se was not that damaging for the development of medical genetics at Charles University, despite ideological fights between Professors Sekla and Hašek. They both were great personalities. Fortunately, ideological implementation of Lysenkoism didn't touch medical genetics development in our country due to its main initial phase of development in the "Golden Era" of the sixties, which I had described to you. Lysenkoism was at its height in the fifties. Nonetheless, Lysenkoism had a negative impact in agriculture, animal breeding research.

Speaking of personalities, Prof. Houštěk as prominent Party member had the courage, approx. 4 years before the fall of Lysenko´s ideology, to establish the first Department of medical genetics at his Institute. One of the first tasks that I got from him was to write an overview of Mendelian genetics and their impact on the development of hereditary diseases for medical students. Frankly, this way I learned about it slightly ahead of them (laughs). As I said he officially supported Mendelian genetics and immediately recognized its impact on the prenatal and postnatal child development, mainly after returning from the visit to USA.

In the critical period of so called political “normalisation” in the early seventies, following the crushing of “Prague Spring”, ended the era of “Golden Sixties”. Prof. Houštěk in his capacity of a Dean did not allow personal discrimination at Faculty of Paediatrics. Remember, at that time a great majority of clinicians were discharged from the Party, due to their protests against Soviet invasion in 1968 to our country. Elimination from the Party also meant that those people lost their managerial positions, academic careers or possibility of PhD studies, and even were threatened by dismissal from respective medical or scientific departments. At our medical faculty this affected only two individuals, but prof. Houštěk hired them back to his research Institute so they could work, publish, virtually do everything as before. However, at other places this situation was far worse.

When the regime recognised how our specialty strengthens “prevention”, which was the major objective of its underlying policy to foster care for “mother and child”, we had received “green light” for all of our activities. Simply, prevention “opened doors”, thanks to this public health objective, soon positioned itself amongst the top countries in vaccination against polio and in rapid decreasing perinatal and infant mortality.

It was the general political notion that we should reach the level and/or do better than Western countries (laughs). The sense of this “competitive ideology” was not that bad, because it served to our people. And especially thanks to these great colleagues I had mentioned, like Profs. Brunecký, Charvát and Houštěk, who directed the development of medicine towards early prevention, even prenatal prevention. They cleverly used the state ideology to improve as best as possible medical care. Therefore, the implementation of prenatal diagnostics was one of the most important facts that facilitated adoption and implementation of the conception of medical genetics into the clinical practice.

In agreement with the already mentioned preventive policy it was declared that the country should also improve social services for young families. Therefore, the government created an “Office for Reproduction” to achieve this goal, which resulted in early seventies in a remarkable baby boom. These children are now called “Husák´s children”, named by the former Party chairman who was in charge at that time. Now Husák´s babies deliver further generations and represent the current backbone of the economically active population in our country. This boom was due to the state policy which provided young people with inexpensive housing and if they had children, generous maternity leaves and free kindergartens, essentially all was done to show the “human face” of socialism which most of the population wanted during the previous decade. Thus, in this respect this policy was fuelling all developments in medical genetics and prenatal care, including diagnosis, prevention and treatment of hereditary disorders.

Prof. Brunecký was also a member of the Party and at that time chairman of the Society of Medical Genetics. When I had returned in 1970 from Houston, I met him in Brno and he told me: “We all were expelled from the Party, because of our opposition of the Soviet invasion and support of the Prague spring, while you just returned from USA. Therefore, you have the professional and political credit, your duty is to stay in the Party, accept the function of the Scientific secretary of our Society and protect medical genetics and us from expected political discrimination” This discussion convinced me to remain in the Party to carry out this goal, despite the fact that after Baylor I wanted to concentrate more on science rather than organisation work.

The Society of Medical Genetics played very important role designed by Prof. Brunecký in this critical period. The president of this Society Prof. Otakar Štark and other Board members remained in the Party, except my postgraduate student Dr. Goetz who was discharged from Party. He served as my Administrative Assistant in my function of the Scientific Secretary. One of the members of the Society suggested that we establish within its Board a “Communist Unit”. First we thought that this is rather ridiculous, but since at that time decision of Party units according Party rules had to be “100% respected” and implemented. Our actions were in line with writer Jaroslav Hašek´s philosophy, so

well described in his famous book “The Good Soldier Švejk” (laughs). We found the way how to fight against totalitarian Party discrimination by using its own strategy!

Thanks to it we successfully defended members of our Society in the case of political discriminations. I remember that eg. in Hradec Králove the Chairman of the local medical genetics department had problems in defending his position. Therefore, the party unit prepared a written document, that after careful analysis of the objections against him the Party Unit of Czech Society of Medical Genetics decided that he is a respected good professional and that he should not be discharged, and it really worked out!

Another serious case was solved by this “strategy”. One member of our Society complained to the Ministry of Health, that our co-worker Prof. Seemanová discredited our country, and the Communist system, by reporting the previously mentioned study on the genetic load in our population due to incest and consanguinity. The Society Board and the Party Unit invited the accuser to justify their complaints. We naturally denied the validity of this accusation and our decision was then also valid for Ministry of Health, and prevented any further sanctions against her. Usually political discrimination was misused by some individuals to promote their careers by “eliminating” their better competitors, as documented in this case. I can confirm that Prof. Štark and all members of the society Board fulfilled not only these important political goals, but also professional duties associated with their functions.

I tried to follow the example of Prof. Houštěk as the Chairman of the Department of Medical Genetics at University Hospital Motol. It was very difficult to travel abroad for long term stipends, and practically impossible for discharged Party members. Thus, in order to arrange a fellowship for my postgraduate student Dr. Goetz at the laboratory of Prof. Anne Chandley I persuaded the responsible Party officer that his stay, where he will learn new methods for gamete examination, is some sort of “economical espionage” and that methods transferred back to us will save lot of money. It again may sound absurd, but this strategy was successful.

Nonetheless, despite being a Party member I was also considered as being “suspicious”. In my role of Scientific Secretary of our genetic society I had organized workshops with the highest number of foreign invited lecturers. Once, Prof. Houštěk discretely informed me that I should to be careful since all my phone calls were monitored because of this. Moreover, as a member of the Party I was several times in early seventies disciplined since I did not respect the discriminatory politics of Party at my Department. This was due to fact that my PhD student Dr. Goetz, eliminated from the Party, repeatedly had travelled to Moscow to develop experimental chromosomal mutagenesis, and since I defended the completion of his PhD thesis.

I also remember that one from my postgraduate students, associated with a high ranking Prague Party representative, included in an otherwise good thesis a chapter which was a plagiarism. When I found out I asked her to eliminate this chapter, despite the fact that some colleagues warned me to avoid political repercussions due to her “high level connections”. In the end nothing had happened to me due to the support of Prof. Houštěk who above all valued scientific integrity.

The policies of this adverse “normalisation regime” gradually dissipated throughout the eighties, and the already mentioned 1980 medical genetics conception has allowed us an “unhindered” development. Therefore, I could install Dr. Goetz as a senior health care consultant at my Department already in mid-eighties.

PH **Good.**

MM Here, I just want to add that the son of my relatives wanted to study at the technical university. Party officials in a small town did not recommend it, because he was from a very religious family, and had been visiting regularly church services. So he had to start working in a nearby factory. Party Unit at this factory realised his potential and recommended his studies, even with factory financial

support! These stories just document how personal integrity of people was important to avoid stupid political discrimination and harm.

I want to stress that I do not want by any means to somehow "glorify" my activities in this respect. It was my duty to defend dignity, fair play.

In the fall of 1989 we all supported change of the regime, presuming that there could come another Prague Spring, we hoped for true democracy and expected that good things, such as social advantages, of the old system would be preserved. With the fall of the regime I ended also my membership in the Party. I felt that I fulfilled my goals, which justified my membership. You could believe me, that I never used this membership for any personal profit.

PH And when the regime changed what effects has it had directly on medical genetics in this country?

MM The new regime preserved previous organisational, regional structure of genetic services, all academic departments of medical genetics were also preserved. Some centres successfully became privately owned (Dr. David Stejskal), and new genetic departments had been created. Society of Medical Genetics, Cytogenetic section of the Biological Society and others, have successfully continued their previous activities. Gradually several academic centres and even some private facilities had achieved international recognition and followed upon collaborations developed from the sixties to the late eighties.

Research activities have been supported by the grant scheme of the Czech Ministry of Health, Academy of Sciences, including other State research grant agencies. Newly there was the possibility to apply for foreign funding from EU framework programmes, Norway Grants, including the support from other international grant bodies such as Wellcome Trust (Prof. Viktor Kožich) or US NIH collaborative projects.

System of postgraduate medical genetics education has retained its high standard, both for nurses, laboratory specialists and doctors. International scientific cooperation, availability of international fellowships became accessible, as well as, the exchange of experience and presentation of our results at international congresses. I am proud to say that our Paediatric faculty, which was transformed into the Second Medical School of Charles University in mid-nineties, was the first to include medical genetics as a compulsory one week long subject in pre-graduate medical education.

Thus, everything which we started in the sixties has been developing rather successfully. We also maintained very good working relationships and cultivated personal friendships with our Slovak colleagues after the 1993 peaceful split of Czech and Slovak Federation. Also collaboration with Russian colleagues continued very successfully in EU scientific projects in medical genetics as mentioned COPERNICUS I and II programs.

As a former Party member with the change of the regime I lost the possibility, to remain at the position of a Department chairman. I can assure you that it was a great relief for me (!), since I could return back to "the bench", start publishing again, without the demanding administrative burden.

My successor became Prof. Seemanová top specialist in genetic counselling and dysmorphology. I handed over to her the Center of Medical Genetics with more than 50 staff, with well-equipped cytogenetic, tissue culture and molecular genetics laboratories. This function was later passed to Prof. Goetz, who is specialised in medical cytogenetics and pre-graduate medical student´s education in medical biology and genetics. Since January 2006 this responsibility is now with my son, Milan Jr.

Another of my postgraduate students, now Prof. Dipl. Ing. Zdeněk Sedláček, contributed significantly to the development of molecular genetics in our department. I was happy to arrange for him fellowships at top molecular Institutes in Germany and London. Now he is chairing the Unit of Biology that is part of the current Institute of Biology and Medical Genetics, created in mid-nineties

by an administrative merger of Department of Biology with the our Centre of Medical Genetics. Zdeněk is now very much involved in the molecular genetic studies of hereditary cancer and intellectual disability.

In the nineties I had also focused on the improvement of prenatal diagnosis of cystic fibrosis by biochemical methods, utilising detection of gamma-glutamyltransferase in amniotic fluid in collaboration with an excellent biochemist Prof. Helena Tomášová and Prof. Věra Vávrová CSc, the "great ladies" of prenatal biochemistry and cystic fibrosis, respectively. Věra later became one of the awardees of the European Cystic Fibrosis Society for her life-long research and clinical achievements.

Molecular genetics diagnostics were introduced at our Department by my son Prof. Milan Macek Jr., thanks to his stipend at Free University in Berlin at the Prof. Karl Sperling´s Institut für Humangenetik (1989-1992) and afterwards at the McKusick Nathans Institute of Genetic Medicine of the John Hopkins University in Baltimore (1992-1995), in the group of Prof. Garry R. Cutting. My "historic" evaluation of his cystic fibrosis genotyping results in various European populations led to the hypothesis of Celtic origin of CFTR mutation G551D and the Paleolithic origin of CFTR mutation deltaF508, later confirmed in Nature. Results of these studies were recognised by the third Scientific Award of Ministry of Health.

I have to remember that I realized the Prof. Houštěk´s idea on the importance of long term studies of disorders of the child development. I sampled and archived newborn-, adult- and octogenarian blood samples for the study of a possible selective advantage of CFTR mutation carriers, including its gene-linked variants. The most important outcome of this study was the discovery of the first gene, termed Klotho, related to human aging .as joint work with Prof Cutting´s group, including Milan Macek Jr. and Alice Macková-Krebsová (my daughter) as his postgraduate and pregraduate students, respectively. This study was published in PNAS USA.

I had introduced QF-PCR for rapid prenatal diagnosis of common chromosomal aneuploidies. We were the first in the country to introduce biochemical screening in the I. trimester of pregnancy due to our cooperation with Prof. Howard Cuckle from Leeds.

In 1995 I established the Centre of Reproductive Genetics at our Department which I considered as a logical extension of prenatal diagnosis to preimplantation genetic diagnosis. In this field we have been collaborating with prof. Markus Montag from Bonn, and with our wonderful colleagues and friends from SiSMER Institute in Bologna – Prof. Luca Gianarolli and Dr. Cristina Magli. I also utilised my expertise in long term cultivation of human tissues for the cultivation of children solid tumours for cytogenetic examination with interesting findings documenting the association of speed of cancer cell outgrowth from operation biopsies in vitro with the degree of malignancy. We could also improve molecular cytogenetic methods for prenatal diagnosis due to our cooperation with Prof. Frank Pellestor from Montpellier.

In 2001 I organised in Prague the international conference on "Early Prenatal Diagnosis, Foetal Cells and DNA in the MotheMM Present Status and Perspectives". Proceedings from this conference, including our own studies, were published in 2002, monograph and were edited by myself, Prof. Diana W. Bianchi from Boston and Prof. Cuckle. We also organised multiple workshops related to our EU-funded projects, ESHRE in 2005 with Milan Jr. at our Department. We also organised the 2005 ESHG conference with Milan Jr. in Prague.

Since 2000 and until my expected retirement at the end of 2013 I decided to concentrate on reproductive molecular genetics by studying FSH, LH and androgene receptor polymorphisms in association with the ovarian hyperstimulation syndrome, individualisation of hormonal stimulation in assisted reproduction, or with regards to the progression of hormone-dependent tumours. We studied also protamine gene variants in male infertility in collaboration with Prof. Frank Tüttleman from Münster with kind support of Prof. Manuela Simoni from Modena.

After 1990 I became the main research “fundraiser” of our Department (laughs). In the last two decades I assured research and structural funding of over 500 million CZK, and important EU grant, for recently completely renovation the laboratory section of the Department from European Social Funding (OPPK) and introduction of next generation sequencing in research and diagnostics. I was really pleased to contribute to all this up to my early eighties, in fact research and daily work at the Department became my “anti-ageing” remedy. I still enjoy teaching of medical students in medical genetics and reproductive genetics and medicine.

During my professional life I was sincerely happy and have remained enthusiastic all the time. I was stimulated and inspired by top scientists, whom I had a chance to meet and learn from them. So this is the answer to your question (laughs). I am happy that I can say this!

For me it’s a message that even if everything has not developed as one had originally intended, you could still remain happy knowing you tried as best as possible to be useful for others. This is another plagiarism to paraphrase the motto of King John of Luxembourg, father of our famous emperor Charles IV – “Ich Diene”, this means “service for the benefit of others”.

My life long „plagiarism” has been to “copy” the example of my parents, how they lived, worked and struggled in difficult periods of their lives, not to be afraid to do good, and not to do bad things throughout my life. Just recently, I recognised that this idea was originated by Confucius to make a better World.

I am happy to be one of a large group of colleagues who built up genetics in our country. I unfortunately cannot name all of them here. Finally, we are not ashamed of historical developments of medical genetics in our country, which should be considered within the overall political and social post-WWII context.

PH **Well thank you very much, Milan. I’ll stop the machine there because we’ve spent a lot of time. But thank you very much for telling me your story. Thank you!**