EAA Andrology Training Centre

Centre Report

2020

Centre identification
School of Medicine University of Zagreb/University Hospital “Zagreb”
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Director of the Centre: Prof. Dr Davor Ježek

CENTRE REPORT

History of Centre

Although the EAA training centre Zagreb (Croatia) has been certified in 2016, reproductive medicine started to develop almost 60 years ago under the auspices of the School of Medicine University of Zagreb and University Hospital "Zagreb". At the beginning of 1953, at the Clinic for Gynaecology and Obstetrics, the outpatient clinic for the treatment of sterility was established. It was the first organized activity to investigate and treat infertility in Croatia and the wider region. With the development of the medical profession and staff, a new department aroused: Department of Gynaecological Endocrinology and Sterility (1962) followed by the Centre for Gynaecological Endocrinology and Fertility (1977). Finally, in 1988 (up to the present time) the Centre was transformed into the Department of Human Reproduction. From the very beginning, the Department has a well-established andrology laboratory that is subjected to both internal as well as external quality control. Six years later, the Department becomes a reference centre of the Ministry of Health and Social Welfare of the Republic of Croatia. The EEA training centre Zagreb and Department of Human Reproduction are strictly collaborating and are involved in a series of important activities, some of them listed in a chronological order: children and adolescent andrology and gynaecology (1967-1970); research and treatment of amenorrhea and intersexualism with the determination of the karyotype; new interpretations of the Morris syndrome, menopause praecox and gonadal dysgenesis (1962-1970); complex corrective surgery of abnormal sexual organs including hypo- and epispadias, vaginal aplasia, uterus duplex (1974); establishment of the Family Planning Centre (1978); foundation of the Centre for IVF and other methods of assisted fertilization (1982); beginnings of in vitro fertilization (IVF) (1982) with the the first baby born with IVF (1983) (7th centre in the world); foundation of the outpatient clinic for sexually transmitted diseases (STD) (1986); embryo cryopreservation (1992); first application of intracytoplasmic microinjection of spermatozoa - ICSI (1994); introducing biopsy of the testis/ testicular sperm extraction / TESE / and TESE/ICSI procedure (1996); vitrification of embryos (2005) and oocytes (2009); application of oncofertility procedures (2011); establishing of the first Testicular tissue biobank at the level of Republic of Croatia (2013).

Today, all forms of research, diagnosis and treatment of male infertility are being applied in the EAA Training Centre Zagreb. In 2017, advanced methods of diagnosing DNA damage in spermatozoa have been introduced. The treatment of infertility is additionally accomplished by identifying ovarian reserve, risk of ovulation stimulation, and possible factors that reduce fertility and success of IVF. Modern approaches to andropause, contraception, gynaecological endocrinology, paediatric and adolescent andrology and gynaecology, as well as perimenopausal medicine, have been introduced. Overall, 15 clinical departments/clinics of the University Hospital "Zagreb" are included in the health care of the infertile couple. Leading role play Clinics for Urology and Gynaecology and Obstetrics. EAA The current director of the EAA Training Centre Zagreb is Prof. Dr Davor Ježek (EAA academician) and the clinical responsible is Prof. Dr Željko Kaštelan, the Head of Clinic of Urology.

Organization of Centre

EAA "Zagreb" is part of the University of Zagreb School of Medicine and University Hospital Zagreb (KBC "Zagreb"). KBC "Zagreb" functions as an umbrella health institution in the Republic of Croatia and is recognized by the Ministry of Health as a hospital of the highest category. For decades, the hospital has a strong tradition in providing health services in the field of reproductive medicine and andrology. Given the complex nature of diagnostic, therapeutic and diagnostic-therapeutic procedures in the field of reproductive medicine, as many as fifteen clinics and clinical institutes of KBC "Zagreb" form a kind of intertwined network that function within the EAA training centre Zagreb (please, see the ORGANIZATIONAL CHART). These are the following clinics and clinical institutes:

Urology Clinic

Clinic for Women's Diseases and Obstetrics

Clinic for Internal Medicine

Clinic for Dermatovenerology

Pediatric Clinic

Clinic of Neurology

Oncology Clinic

Clinic for Cardiovascular Diseases

Psychological Medicine Clinic

Clinic for Anesthesiology, Resuscitation and Intensive Care

Clinical Department of Transfusion Medicine and Transplant Biology

Clinical Department of Pathology and Cytology

Clinical Institute for Laboratory Diagnostics

Clinical Department of Clinical and Molecular Microbiology

Clinical Department of Diagnostic and Interventional Radiology.

The key role in the EAA training centre Zagreb plays the Clinic for Urology. The Clinic is the largest urological institution in the Republic of Croatia and takes care of urological patients from all parts of the country. In addition to caring for urological patients, the Clinic is a place where specialist and subspecialist training in the field of urology and andrology is performed.

Under the auspices of the Clinic, in addition to several reference centres of the Ministry of Health, there is also EAA Center. In the operational theatre 2 (URO2), the Clinic of Urology has the necessary equipment to perform an open testicular biopsy that is part of the procedure of medically assisted fertilization. In cooperation with the Department for Transfusion Medicine and Transplantation Biology (Testis biobank) and the Clinic for Women's Diseases and Obstetrics, a complex diagnostic-therapeutic procedure TESE / ICSI is performed. Besides, penile and urethroplasty techniques and treatment of erectile dysfunction have been developed within the Clinic.

At the uro-oncology department, patients are provided with a full range of diagnostic and therapeutic procedures in the treatment of various types of urological diseases (stones, BPH, etc.), with special emphasis on the treatment of patients with malignant urological tumours. The most complex oncology patients who need an individual and multidisciplinary approach are treated here. The operative program covers tumours of all urological organs: kidney, ureter, bladder, prostate, testis and penis. Procedures performed in such patients reflect modern guidelines in urological surgery and include radical tumour nephrectomy (removal of the kidney with the tumour), partial nephrectomy (removal of the tumour while preserving part of the kidney), radical nephroureterectomy (removal of the kidney and prostate), radical cystectomy

(removal of the bladder) with all forms of urine drainage, radical orchidectomy (removal of testicles with a tumour), and surgical procedures for penile tumours. The Prostate Center is a functional unit of the Urology Clinic, opened on December 19, 2016. Its main function is to simplify the process and shorten the time required for diagnostic processing and treatment of prostate disease. In 2019, the Clinic obtained robotic surgery equipment for advanced urology and abdominal operations.

For many years, the Clinic of Urology of the University Hospital Center Zagreb is the largest centre for kidney transplantation in the Republic of Croatia, and after our country joined Eurotransplant in 2007 and achieved top results in transplant medicine, it became a central place for education in the field of kidney transplantation. The Clinic of Urology is particularly developing transurethral techniques of minimally invasive procedures. Transurethral endoscopic technique is used in the treatment of benign prostatic hyperplasia, bladder cancer, urolithiasis, etc. With excellent collaboration with endocrinologists, nephrologists and oncologists, patients are provided with a wide range of laparoscopic surgeries. More than 100 laparoscopic procedures are performed annually at the Clinic. Examples of such procedures are laparoscopic adrenalectomy, laparoscopic retroperitoneal lymphadenectomy (determination of disease stage or after chemotherapy as part of the treatment of patients with the testicular tumour), laparoscopic and retroperitoneal nephrectomy, radical nephrectomy and other interventions.

Educational activities

EEA Training Centre Zagreb participates in the graduate education of students of medicine in 2 study programmes: Medical Studies in Croatian language (annual intake: 300 students) and Medical Studies in English (annual intake: 50 students). During the courses entitled Urology and Gynaecology and Obstetrics, essential principles of treatment of infertile male/couple are presented. The Centre also participates in postgraduate education of endocrinologists, urologists and gynaecologists (annual intake: 15-20 postgraduate students per postgraduate programme). EAA Training Centre Zagreb is contributing to PhD studies entitled

Biomedicine and Health where new scientific advances in the area of andrology are presented. The Centre is especially active in sub-specialisation in andrology (in Croatia it is a part of the specialization in urology). Under the auspices of EAA, the Centre organized already two editions of the andrology school entitled "Testis Histology and Pathology for Clinical Andrologists and Embryologists" (in years 2017 and 2019) and three Andrology Symposia (in years 2017, 2018 and 2019). The afore-mentioned andrology school was pursued together with EAA Training Centre in Copenhagen.

Research activities

In 2014, EAA Training Centre was awarded the status of **Centre of Excellence for Reproductive and Regenerative Medicine** by European Commission. The Centre has two research units (for reproductive and regenerative medicine). In the year 2017 the Centre of Excellence was awarded a grant from EU (grant no. K.K. 01.1.1.01.0008, 5 mils. EURO) to pursue with the project entitled "**The reproductive and regenerative medicine: the investigation of new platforms and potentials**" (2017-2022).

Center of Excellence of the Medical Faculty of the University of Zagreb for Reproductive and Regenerative Medicine
The research unit "Biomedical research of reproduction and development"

The research unit "Biomedical Research of Reproduction and Development" of the Center of Excellence of the Medical Faculty of the University of Zagreb was created in response to the health needs of modern Croatian society. It is generally known that in the EU (including the Republic of Croatia) 15% of couples have fertility problems. The recent demographic data point to the fact that there is a very worrying annual deficit of 13,000 newborns in Croatia. For example, only the school year 2012/2013. 130 classes of "first-graders" were enrolled less than a year earlier. It is estimated that 80,000 couples in Croatia are infertile, and only 12,000 couples are treated. There is also a very dangerous trend of delayed childbirth: as many as 31% of Croatian women give birth to their first child at the age of 31-35. years of age and only 14% of couples decide to have a

third child. Epidemiological data in the last 15 years also indicate a worrying increase in infertility in our country of 5%. There is also a higher incidence of testicular neoplasms, the most common tumour of young men aged 15-28 years and congenital anomalies.

All these above-mentioned problems of the younger Croatian population were the motive for gathering a multidisciplinary group of scientists from the basic, clinical and public health fields of reproductive medicine. The research unit, in addition to its headquarters at the Medical Faculty of the University of Zagreb, gathers a wide range of the following institutions and professional societies: University Hospital "Zagreb", Clinic for Children's Diseases in Zagreb, University Hospital "Sisters of Mercy", Clinical Hospital "Holy Spirit ", IMI (Institute for Medical Research and Occupational Medicine), the Croatian Society of Clinical Genetics and the Croatian Society of Human Genetics. The project tasks of the Research Unit (modelled on the FP7 and Horizon 2020 projects) can be roughly divided into basic and translational research and public health actions and training of young researchers. Of course, these studies are intertwined and interconnected and include the following tasks:

1. Investigations of epigenetic markers during the reproduction and development of mammals
2. Epigenetic studies of congenital anomalies
3. Epigenetics and germ cell tumours
4. Biomarkers of abnormal pregnancy
5. FSHR gene polymorphism
6. Human testis and sperm

As can be seen, the focus of the research is on epigenetics. Epigenetic research will include the study of gene expression regulation at the level of DNA methylation - reversible genetic changes that are both hereditary and can be modified by lifestyle. Such regulation is necessary for the normal development of gametes, embryonic stem cells, embryos and placenta, so deviation from this can lead to infertility, abnormal placenta development and congenital anomalies. Epigenetic changes play an important role in the initiation and development of tumours and other human diseases. Specific epigenetic markers detected in various disorders may serve as biomarkers with prognostic values. Epigenetic therapy is already available today.

Besides, the Centre conducts studies on animal models and different human populations using genetic and non-genetic methods and provides a link between basic research on reproduction and development of mammals (conducted on animal models in vivo and in

vitro) and clinical research on male infertility, placental dysfunction, congenital anomalies and genetic disorders. This will enable two-way translation, basic research towards problems in medical practice and vice versa. Of particular importance is the study of the environmental impact on the mother and newborn through a multidisciplinary approach involving genetic, epigenetic, immunological, genotoxicological and endocrine biomarkers, which will be analyzed and interpreted by complex multiparametric analyzes.

Translational research includes the improvement of some forms of clinical practice of reproductive medicine. Efforts will be made to introduce the method of freezing and cultivating spermatogonia as a kind of stem cells which, if modified and autotransplant, can restore spermatogenesis in an infertile man. Particularly important translational research will focus on oncofertility. It is planned to introduce a tissue bank of immature gonads of girls and boys with malignant diseases as well as mature ovaries to store gametes for future autotransplantation before chemo and radiotherapy.

Public health and other actions intended to be taken include the printing of educational leaflets describing the self-examination of the testicles.

A project of Croatian research fund: EPI-SEM

In 2017, Croatian agency for research awarded the EAA Training Centre Zagreb with the project entitled "**Epigenetic biomarkers in blood and ejaculate in patients with seminoma**" (duration of the project: 48 months, budget 978.000,00 kn (128.684 EURO).

Testicular germ cell (TGCT) tumours are the most common tumours of the younger male population in the world. Our epidemiological study from 2011 showed the highest trend of increasing incidence rate in the world and high mortality in the Croatian population. "Model-based" research on risk trends and demographic trends from 2014 highlights the Croatian population as one of the three most vulnerable in Europe and predicts that in Croatia by 2025, one in 100 men will be diagnosed with TGCT per year. Seminoma is the most common type of TGCT, with a trend of further increase. Both (micro) environmental and (epi) genetic factors are thought to lead to its development. Today, epimutations of DNA methylation stand out as tumour biomarkers due to their high frequency and pronounced chemical and biological stability, which gives them an advantage in the development of non-invasive

diagnostics. It is precisely the research of biomarkers from body fluids that is strongly encouraged today as this concept is considered one of the foundations of personalized medicine. The proposed prospective study hypothesises that biomarkers of seminoma at the level of free DNA methylation can be identified in blood plasma and ejaculate. In parallel with the anamnestic and clinical treatment, a comprehensive study of DNA methylation will be performed on samples of patients before and after therapy and the results will be compared with samples of healthy men. Comparison of free DNA and tumour DNA methylation results, as well as variations in gene copy number, will clarify the proportion of tumour DNA in body fluids, eliminate background free DNA noise from healthy tissue, and show the impact of genomic aberrations on informative free DNA methylation analysis. Comparison of these results with protein expression of the examined genes in seminomas in samples of the same patients will clarify the relationship between the methods of modern molecular pathology and the proposed new approaches in the development of personalized medicine. Scientific contribution in the field of development of epigenetic biomarkers in body fluids of oncology patients is expected.

A project of Croatian research fund: EPI-PRO

In 2018, Croatian agency for research awarded the EAA Training Centre Zagreb with the project entitled "**Epigenetic markers of prostatic carcinoma**" (duration of the project: 60 months, budget 2.100.000,00 kn (276.315 EURO).

Epigenetic disorders can be identified extremely early in the development of human disease and represent a dynamic area of research for potential biomarkers. Awareness of the competitiveness of epigenetic research is slowly developing in Croatian science, which is recording a decline in prostate cancer (RP) research. However, RP is the second most common cancer and the third leading cause of death in men from cancer in the Republic of Croatia, the incidence of which is growing steadily, as well as mortality. It is thought that epigenetic biomarkers (EB) would allow for earlier diagnosis and a higher survival rate. Methylation of DNA and microRNA (miRNA) stand out as EB, and several EB prostate cancers have been identified in tumour tissue research. This research is based on the latest concept in the development of EB in the

framework of male reproductive health - EB research in the causes of liquid biopsies, i.e. in ejaculate and blood.

RP-associated genes and miRNAs were selected for molecular analysis in accordance with the latest findings in the literature. In the semen and blood of patients with RP, non-cellular DNA methylation profiles (cfDNA) will be determined by pyrosequencing, and miRNA expression by qPCR or ddPCR. Epigenetic and expression profiling will also be performed on tumour samples of the same patients. In addition to research activities, the project intends to raise awareness of the benefits of introducing epigenetic issues in established research groups, educate future young researchers and contribute to the development of non-invasive diagnostics of RP. Therefore, a new multidisciplinary Group for the Research of Epigenetic Biomarkers (epiMark) was established within this project.

Clinical activities

Clinical activities & techniques are as follows:

- Semen analysis
- Comprehensive endocrinological analysis
- Outpatient clinic (andrology + endocrinology)
- Outpatient clinic for sexually transmitted diseases (STD)
- Outpatient clinic for infertility couple
- Outpatient clinic for psychological counselling of infertile couple, gender dysphoria, erectile dysfunction etc.
- Management of erectile dysfunction
- Ultrasound of the testis, prostate, accessory glands, retroperitoneal lymph nodes etc., CT and NMR facilities
- Genetics of male infertility (karyogram, Y chromosome microdeletions (including extended analysis), CFTR
- Comprehensive microbiology analysis
- TESE, m-TESE

- Histology of testicular biopsies
- IVF facility applying advanced ART including programmed and snap freezing
- Management of varicocele
- Prostate centre (BHP, US, biopsies, laparoscopic and robotic surgery)
- Management of testicular neoplasms (uro-oncology team)
- Penoplasty and penile prosthesis
- Vasectomy & vasectomy reversal

Name and address of Centre

European Academy of Andrology Training Centre ZAGREB
School of Medicine University of Zagreb/University Hospital "Zagreb"
Šalata 3, HR-10000 Zagreb/Kišpatićeva 12, HR-10000 Zagreb, Croatia, EU
Phone/Fax.: +385 1 45 90 251

Type of Centre

University	X
University Hospital	X
Private Centre	

Other (please specify)

1. Director Prof. Dr Davor Ježek, M.D.

Academician [X] Affiliated Member [ ] Clinical Andrologist [ ]

2a. Clinical responsible Prof. Dr Željko Kaštelan, M.D.

Academician [ ] Affiliated Member [ ] Clinical Andrologist [X]

2b. Clinical responsible Dr Dinko Hauptman

Academician [ ] Affiliated Member [X] Clinical Andrologist [X]

2c. Clinical responsible

Academician [ ] Affiliated Member [ ] Clinical Andrologist [ ]

3. Present Staff *(Senior Scientists)*

1) Name: Nino Sinčić
Degree: Associate Prof., M.D.
Speciality: Medical genetics

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

2) Name: Ana Katušić Bojanac
Degree: Associate Prof., biologist
Speciality:

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

Insert any additional staff below *(if required)*

MD/Biologists/Chemists

1) Name: Zoran Zimak
Degree: M.D.
Speciality: Urology (sub-specialisation andrology, in the process)
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

2) Name: Nina Pleša Gelo
Degree: Ph.D., Biologist
Speciality: Clinical embryology
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

3) Name: Mihajlo Strelec
Degree: M.D., PhD.
Speciality: Gynaecology and Obstetrics (subspeciality human reproduction)
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

4) Name: Dinka Pavičić Baldani
Degree: Full Professor, M.D., PhD.
Speciality: Gynaecology and Obstetrics (subspeciality human reproduction)
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

5) Name: Lana Škrgatić
Degree: Assistant Prof., M.D., PhD.
Speciality: Gynaecology and Obstetrics (subspeciality human reproduction)
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

6) Name: Maja Banović
Degree: PhD., M.D.
Speciality: Gynaecology and Obstetrics (subspeciality human reproduction)
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

7) Name: Hrvoje Vrčić
Degree: Associate Prof., M.D., PhD.
Speciality: Gynaecology and Obstetrics (subspeciality human reproduction)
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

8) Name: Marina Šprem Goldštajn
Degree: Associate Prof., M.D., PhD.
Speciality: Gynaecology and Obstetrics (subspeciality human reproduction)
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

9) Name: Gabrijela Kirinec
Degree: PhD. , Biologist
Speciality: Clinical embryology
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

10) Name: Marija Vilaj
Degree: Biologist
Speciality:
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

11) Name: Saša Kralik
Degree: PhD., Biochemist
Speciality: Medical Biochemistry
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

12) Name: Tina Dušek
Degree: Assistant Professor
Speciality: Internal medicine, Endocrinology
Full time/part time: Full time

Academician ☐ Affiliated Member ☐ Clinical Andrologist ☐

Insert any additional staff below *(if required)*

Specialists

1) Name
2) Name
3) Name
4) Name
5) Name

PhD Students

1) Name Ana Planinić
2) Name Dora Raos
3) Name

Nurses

1) Name Ivanka Kolačević
2) Name Ivanka Gelo
3) Name Đurđica Zlodi

Laboratory Technicians

1) Name Suzana Tutić
2) Name Melanija Holi
3) Name Tomislav Popović

Administrative Personnel

1) Name Barbara Kalenić
2) Name Željka Topolovec
3) Name

4. Clinical Activity

A. Outpatients: Consultations per year in the last 3 years

	2017	2018	2019
New patients	523	561	544
Follow-up patients	239	216	223

Type of patients in the last years (%)	2017	2018	2019
Infertility	142	153	171
Erectile dysfunction	31	26	33
Hypogonadotropic Hypogonadism	1	0	2
Klinefelter	4	5	4
Gynaecomastia	0	2	0
Varicocele	12	14	11
Cryptorchidism	0	0	0
Male sex accessory gland infections	12	15	9
Testicular tumours	4	3	5
Disorders of gender identity	0	1	0
Other			

B. Ultrasound (testis, penile, prostate) *

	2017	2018	2019
Total	420	358	433
Controls	154	98	187

** performed at the Department of Radiology*

C. Andrological surgery procedures

	2017	2018	2019
Testicular biopsies	39	52	51
Varicocele ligation	29	32	27
Prostate biopsies	329	353	360
BPH	128	136	131
Prostate cancer	92	125	142
Vasectomy	0	2	0
Vaso-vasostomy	0	0	0
Other			

5. A. Andrology laboratory activity

	2017	2018	2019
Semen analyses	1807	2132	2205
Sperm antibodies	0	0	0
Seminal markers	1734	1832	1729

5. B. Andrology laboratory activity

Sperm banking donors Yes [ ] No [X]

Sperm banking cancer patients Yes [X] No [ ]

If yes:			
	2017	2018	2019
Number of samples	56	51	64

5. C. Histopathologial evaluation of biopsies Yes [X] No [ ]

5. D. Reproductive Hormones Assays Yes [X] No [ ]

If yes please specify the type of assays and number of samples in the last year
Reproductive Hormones Assays
(FSH, LH, testosterone, SHBG, prolactin)
FSH, LH, T, SHBG, DHEA-S, Hcg, prolactin - 2521

5. E. Y chromosome microdeletions according to EAA/EMQN guidelines Yes [X] No [ ]

If yes number of tests in the past year 242

Participation to the EAA quality control scheme? Yes [X] No [ ]

If no, specify if available in another lab of the same hospital Yes [ ] No [ ]

Blood karyotyping Yes [X] No [ ]

If no, specify if available in another lab of the same hospital Yes [ ] No [ ]

Other genetic tests (please specify)
FISH sperm **Yes**
Pre-implantation genetic diagnosis **No (in preparation**)
Amniotic fluid karyotyping **(Yes)**

6. Collaborations with other Clinical Units of the University/Hospital

IVF Unit Yes [X] No [ ]
If yes please specify: Children, Endocrinology, IVF, Urology, Genetics, Pathology

Urology Clinic Yes [X] No [ ]

Endocrine Clinic Yes [X] No [ ]

Genetics Lab/Unit Yes [X] No [ ]

Paediatric Unit Yes [X] No [ ]

Central Hospital Laboratory Yes [X] No [ ]

Private Centres Yes [X] No [ ]

If yes please specify:
Providing private IVF centres with testicular biopsies upon the request of infertile couple and approval of the National Commission for medical fertilization (appointed by the Ministry of Health).

7. Clinical teaching activity
Duration of training (years): 5

	Number
A: Trainees in the last five years	82
B: Trainees who passed EAA-ESAU\exam for Clinical Andrologist in the last 5 yrs	
C: Trainees working in the centre preparing to pass the EAA-ESAU examination	1
D: PhD Students	8
E: Medical Students	350/annualy
F: Other students (MSc)	0

8. Formal Andrology teaching program Yes [X] No [ ]

If yes: specify duration (years/months): Years [5] Months [ ]

	Hours of formal teaching per year	**Professional training (weeks/months)**
Medical Students	40	2 weeks
PhD Students	120	2 years
Post Graduate students	360	1 year
Trainees	360	5 years
Other degrees (please specify)		

9. Research Activity (maximum 1 page)
Please shortly describe the main research topics of the centre and list the most relevant papers in peer review journals (with IF) related to these activities.

The full report on the research activity of the centre is presented in detail on **pages 7-11**. Here is the list of research topics:

1. Investigations of epigenetic markers during the reproduction and development of mammals
2. Epigenetic studies of congenital anomalies
3. Epigenetics and germ cell tumours
4. Biomarkers of abnormal pregnancy
5. FSHR gene polymorphism
6. Human testis and sperm

The full list of publications (years 2017 - 2019) are presented at the end of this report.

10. Research Funding
Please specify the amount of available funds in the last 3 years and their source (Government, European Union, University, Local Government, Pharmaceutical Industries, Banks, Foundations….)

Year	2017 (Centre of excellence for reproductive and regenerative medicine)
Total amount (€)	5 mil.
Funding Source(s)	EU (grant no. K.K. 01.1.1.01.0008, 5 mils. EURO)

Year	2017
Total amount (€)	128.684,00
Funding Source(s)	Croatian research fund (project: "Epigenetic biomarkers in blood and ejaculate in patients with seminoma")

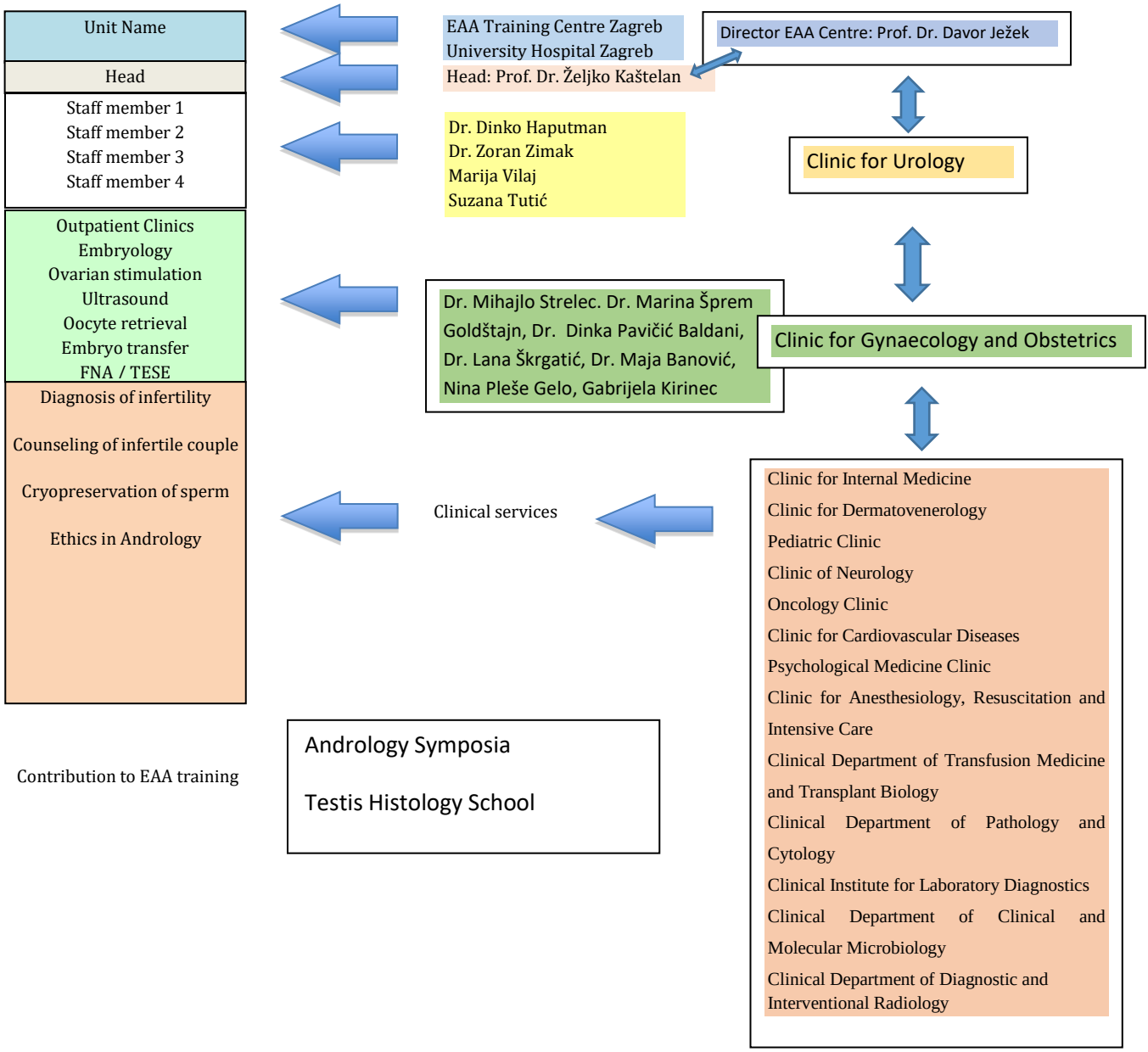
Year	2018
Total amount (€)	276.315,00
Funding Source(s)	Croatian research fund (project: Epigenetic markers of prostatic carcinoma)

Insert any additional funding below if required

2017-2019
-annual grant of University of Zagreb: 6000, 00 EURO

ORGANIZATION CHARTS

Organization charts legend: Department / Unit Structure



CENTRE PHOTOS

FULL LIST OF PUBLICATIONS (with IF) of staff members from the last 5 years

Kastelan Z, Hudolin T, Kulis T, Penezic L, Gidaro S, Bakula M, Zekulic T, Knezevic N. Extraperitoneal Radical Prostatectomy with the Senhance Robotic Platform: First 40 Cases. Eur Urol. 2020 Jul 24:S0302-2838(20)30544-3. doi: 10.1016/j.eururo.2020.07.012. Epub ahead of print. PMID: 32718799. (IF=17.29)

Kuliš T, Zekulić T, Alduk AM, Lušić M, Bulimbašić S, Ferenčak V, Mokos I, Hudolin T, Kaštelan Ž. Targeted prostate biopsy using a cognitive fusion of multiparametric magnetic resonance imaging and transrectal ultrasound in patients with previously negative systematic biopsies and non-suspicious digital rectal exam. Croat Med J. 2020 Feb 29;61(1):49-54. doi: 10.3325/cmj.2020.61.49. PMID: 32118378; PMCID: PMC7063559. (IF=1.247)

Fucic A, Starcevic M, Dessardo NS, Batinic D, Kralik S, Krasic J, Sincic N, Loncarevic D, Guszak V. The Impact of Mother's Living Environment Exposure on Genome Damage, Immunological Status, and Sex Hormone Levels in Newborns. Int J Environ Res Public Health. 2020 May 13;17(10):3402. doi: 10.3390/ijerph17103402. PMID: 32414150; PMCID: PMC7277460. (IF= 2.849)

Plazibat M, Katušić Bojanac A, Himerleich Perić M, Gamulin O, Rašić M, Radonić V, Škrabić M, Krajačić M, Krasić J, Sinčić N, Jurić-Lekić G, Balarin M, Bulić-Jakuš F. Embryo-derived teratoma in vitro biological system reveals antitumor and embryotoxic activity of valproate. FEBS J. 2020 Nov;287(21):4783-4800. doi: 10.1111/febs.15248. Epub 2020 Feb 28. PMID: 32056377. (IF=4.392)

Fucic A, Maric T, Vicic Bockor V, Jezek D. In vivo acridine orange human spermatozoa staining-A new perspective for RNA detection and spermatozoa morphology evaluation. Anat Histol Embryol. 2020 Aug 24. doi: 10.1111/ahe.12606. Epub ahead of print. PMID: 32840006. (IF=0.696)

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