Multi-disciplinary platform for institutional capacity enhancing dermatooncology and dermato-pathology domains

PATHDERM

- Project Director: Prof. Dr. Sabina Andrada Zurac
- Coordinating Institution (CO): Spitalul Clinic Colentina, București
- Domain Health
- Budget: 5.287.148,00 lei
- Key words: dermatopathology, dermato-oncology, multi-omics

Abstract:

Dermato-oncology and dermato-pathology address the most frequent pathology, but the medical training is scarce, hence the new diagnosis and treatment approaches in skin cancers are frugaly tought in residency and in post-universitary training. Thus, the medical act is hindered by the "in-house" training of the clinicians that can lead to low quality medical serivces for the patient. The project re-unites 6 prestigious institutes that have prior collaborated (Bucharest, Cluj): an university hospital, a national institute, a Romanian Academy national institute and 3 universities (two medical ones) that propose for the first time on national level a research and training platform for dermato-oncology and dermato-pathology developing 4 multi-disciplinary projects. Project 1 developps an improved diagnostic and prognostic markers for the most frequent skin cancers- squamous cell and basal cell carcinomas. Project 2 identify the markers for improved prognosis and therapy monitoring in cutaneous melanoma. Project 3 develops new methologies for therapy testing in dermato-oncology and dermato-pathology. Project 4 completes the training slope of young researchers and medical doctors to increase the medical services quality (decrease social costs of the dermato-oncology pathology) and to increase the research results in the biomedical domain. We estimate a significant impact of the results on the institutional capacity consolidation regarding human resources (13 new research positions, several training stages, several work visits) and infrastructure (upgrading of the existent infrastructure); 3 patents, 3 new sets of biomarkers for diagnostic/prognostic/monitoring for the increase of the health care system, RD services, and international visibility improvement.

Participants

Project Coordinator:
Colentina University Hospital, Project Director Prof. Sabina Andrada ZURAC
Partners:
P1. National Institute for Research on Development in Pathology of Biomedical Sciences Victor Babes, Responsible Prof. Hab. Dr. Teodora Monica NEAGU CS I
P2: Institute of Biochemistry of the Romanian Academy, Responsible dr. Gabriela NEGROIU CS I
P3. University of Bucharest, Faculty of Biology, Responsible Prof. Marieta COSTACHE
P4. UMF Iuliu Haţieganu Cluj, Responsible prof dr. Rodica Maria COSGAREA
P5. UMF Carol Davila Bucharest, Responsible conf. Dr. Daniel BODA, CS I

Coordinator (CO): Colentina University Hospital has a long history of involvement in research work, combining medical diagnostic and treatment activities with medical training. Dermatology and dermatopathology in Colentina University Hospital have a long tradition of performance. Clinical Departments and Department of Pathology operate at European standards, with difficult cases across the country being referred to Colentina University Hospital for diagnosis and treatment. Within the Colentina University Hospital, operates CDPC Research Center (POSCCE 7/2007, 71,367,807 lei 2009-2013); more than 100 national projects were initiated in 2013 and 12 international projects (FP7, HIVERA, etc.) were implemented. Research contracts (related to the proposed project, last 3 years): Polifactorial classifier [... in] melanoma PN-II-PCCA 190/2014; Designing and testing a new family of HIV-inhibiting drugs [...] PN-II-PCCA 120/2014; Development of radiopharmaceuticals [...] intended for [...] PET and systemic radiotherapy; PN-II PCCA228 / 2014; European initiative for the prevention of occupational skin diseases, EADV; Development of the European rare and severe psoriasis expert network, EADV. The team involved in PATHDERM consists of researchers with experience in dermatological oncology (professors, asocciate professors, senior doctors) and 2 PhD students with theses in melanoma.
Colentina University Hospital includes in its structure two clinical departments of dermatology; the research center includes several laboratories of Dermatology (https://erris.gov.ro/Dermatology) and Dermato-oncology (https://erris.gov.ro/Dermato-oncology) that are equiped with a modern surgery room, Excimer laser, light source for photodynamic therapy, in vivo confocal microscope VivaScope 1500, dermoscopic documentation and skin lesion monitoring system MoleMax 3. The Department of Pathology includes CDPC laboratories in the research center (https://erris.gov .ro / Anatomo-Pathology) equipped with modern equipment for processing of biological samples for routine histopathological / cytopathological investigations and complexes, including IHC, IFD, FISH / CISH, electronic microscopy, as well as modern microscopes with simultaneous examination; within Colentina University Hospital, the PATHUNIT and PATHOPLUS laboratories are working in partnership with UMF Carol Davila Bucharest and the Institute of Infectious Diseases Matei Balş Bucharest (http://www.spitalulcolentina.ro/anatomie-patologica/en/buton-en2.html http: // www .matei bals.ro/VIASAN/Prosectura/eng/echipamente.html) access being facilitated by formal interinstitutional agreement.

Victor Babes National Institute (IVB) has a prestigious research activity in human pathology (cancer, immune dysfunctions, genetic abnormalities, toxicology, etc.). IVB has been involved in international projects: NATO (No. 982838/2007), FP7-PEOPLE-IRSES-2008 (PIRSES-GA-2008-230816), MNT-ERA NET (No.7-030 / 2010), ESF projects, international clinical trials, the COST network (D16120; D39; D1002), Nanomedicine Platforms. IVB was involved in the implementation of POSDRU no. 31081, Development of dermatology oncology as an integrated line of medical education [...] and an inter-university partnership network. In POSDRU projects 141531, 135760, 58819 and 59497 IVB has trained hundreds of doctoral and post-doctoral researchers in proteomic and genomic technologies implemented in health. In 2016 (www.ivb.ro), IVB published 44 ISI indexed items, out of which 12 articles with IF> 2 in the project area belonging to the team involved in PATHDERM in collaboration with CO, P3, P5. In 2016 IVB filed three patent applications, one (in dermato-oncology) being held by the consortium's team; they have previously patented innovative compounds in dermatological therapy (patent awarded with gold medals at international inventions fairs). The team consists of highly experienced researchers (CSI, CSII, CSIII) and 2 PhD students with doctoral theses in the field (skin carcinogenesis, identification of biomarkers in melanoma and psoriasis). Collaborations with CO: Genomic &

Proteomic Studies in Melanoma Project PNII-PCCA No. 190/2014 with results 15 articles in ISI journals, 14 posters at scientific congresses, 7 book chapters in ed. International. Collaborations P4 & P5 POSDRU no.31081 Development of dermato-oncology [...] IVB (https://erris.gov.ro/ivbro) has modernized its equipment / facilities through the CAMED grant (12 million Euro, 2014) and will use in projects: proteomic analysis: Innoscan 1100 AL microarray protein; VarioSkan Multimode Detector; xMAP array; ELISA line; cell cultures: BSLII facilities, storage in liquid nitrogen, storage at -800C; cellular testing: cellular impedance xCELLigence platinum, flow cytometry BD FACSDiva ™; cell sorter; Electronic microscopy: TEM, cryo-electron microscope (Cryo-EM), correlative electronic microscopy (CLEM), confocal microscopy of super resolving; sanitary-veterinary biobase authorisation no. 222/2016.

The Institute of Biochemistry of the Romanian Academy (IB) acts as Center for Excellence in Education and Advanced Research in the field of Biosynthesis and Protein Functions. IB has published 90 ISI articles (> 2500 ISI quotes in the last 5 years); is involved in EU-funded projects (FP5, FP6, FP7, EEA): H2020 projects: MSCA-RISE-2015RISE; ERA-NET HIVERA (4007/2014 and 53/2016), EEA projects: IZERZ0_142216, RO-NO-2013-1-0022 and RO-NO_2013-1-0047. IB has coordinated over 50 projects in partnership, CEEX and projects with European funds POSCCE and POSDRU with results with strong applicative impact: 12 patents (3 international, 9 national). IB coordinated projects from European funds: EU-PosDRU "Cellular biotechnologies with medical applications"; POSCCE "Strengthening the administrative capacity of IB"; POSCCE "Development of IB research infrastructure [...]" Collaborations with CO and P5: projects: MelanomaTRP2 (2011-2016), Melaspot (2006-2008), EU- PosDRU "Cellular bio-technologies with Medical applications" 213), papers in ISI indexed journals, presentations at congresses, laboratory procedure transfer (from IB to SCC), patent No. 123570/2013, inventors Negroiu G, Filimon A [...] Zurac S [...] in the course of transferring to Merck-Millipore, who has asked for marketing, IB has extensive experience in the study of tumor and antigens and the ability to exploit and disseminate (h-index 15, 38 articles, 9 patents). to international standards through a POSCCE project (28,448,000 lei, 2010-2012) Facilities of the IB (https://erris.gov.ro/Department-of-Molecular-Cell) to be used in the project: the collection of human and murine melanoma lines (various stages of RGP, VGP, metastatic), melanoma tracing and manipulation, cellular process analysis (proliferation by CFSE and FACS labeling; cell cycle analysis; apoptosis: annexin V + PI; invasiveness / invasion of matrigel; zymography), immuno-cyto / histo-fluorescence / simultaneous labeling for 2 antigens and histopathological section analysis; TissueFAXS - imaging cytometry - allows quantitative analysis of labeled (chemo - / - fluorescent) antigens in cytological or histological samples, CRISPR / Cas9 for DCT - was tested on 2 melanoma lines; the selected clones were validated for the expression of DCT (WB) and ready to be tested further.
The University of Bucharest (UB) through the Department of Molecular Investigations (DIM) of the Platform of Biology and Systemic Ecology developed at international standards through the ESF project POSCCE 915/14043 (2010-2015) conducts fundamental and applied research in Biochemistry and Molecular Biology; national projects for tissue engineering and regenerative medicine (PCCE248 / 2010, PCCA140 / 2012, PCCA130 / 2014), bilateral cooperation, twinning project applications and HORIZON 2020 applications, ESF projects POSCCE 915/14043, COST network (CA-16120 European Epitranscriptomics Network; CA-15205 Gene Regulation Knowledge Commons). The national network of researchers involved in CA-16120 is based on collaboration between UB / IVB teams. UB has extensive experience in the formation of young researchers: POSDRU / 88 / 1.5. / S / 61150, POSDRU / 81 / 3.2 / S / 55362, POSDRU / 159 / 1.5 / S / 133391, POSDRU / 89 / 1.5 / S / 58852 . The

human resource involved includes 3 highly experienced researchers in the field, 6 post-doctoral students, 2 PhD students. Collaborations with P2 training activities: IVB staff - target group in POSDRU / 159 / 1.5 / S / 133391. UB (http://erris.gov.ro/DMI-PCBE) has a generous infrastructure that allows for cellular and molecular biology studies built through the ESF project POSCCE 915/14043 (~ 10 mil euro) inaugurated in 2015. In the project will use: (1) ultramodern cell culture laboratory class ISO8 and BSLII; (2) gene expression assay: qPCR (ViiA ™ 7 Real-Time PCR System), microarray (Agilent), microfluidic single cell cell analysis (C1 & Biomark single cell); (3) new generation sequencing (Life Technologies Ion Proton, Ion PGM); (4) microscopy: Reversed Fluorescence Microscope (Olympus IX73) and Nikon A1 / A1R Confocal Microscope; (4) flow cytometry (Gallios); (5) laboratory histological evaluation; (6) functional biochemistry laboratory.

The University of Medicine and Pharmacy "Iuliu Haţeganu", Cluj (UMFC) is the oldest medical institution in Transylvania with the fastest development in the field of research; it addresses a wide range of research topics: translational, genomic, proteomic, nanomedicine, biomarkers, pharmacology, drug development, etc. In the last 5 years UMFC has implemented projects worth 75,242,201.56 lei. In 2015, UMFC established the Center for the Excellence in Dermatology. Research on keratinocytes, fibroblasts, clinical research in melanoma, determination of the role of metalloproteases in melanoma progression, porphyrin efficacy in cutaneous cancer, molecular diagnosis in bulous epidermolysis were carried out within this research laboratory. Collaborations with P5 and P2: POSDRU no.31081, Development of dermato-oncology [...], ISI publications with the CO team. The Infrastructure of the Center for Excellence in Dermatology oncology carries out diagnosis and treatment by modern methods of dermatologic-oncological diseases: dermatological surgery including Mohs surgery, photodynamic therapy, dermoscopy follow-up of patients at risk of melanoma and molecular diagnostic techniques in dermatology (https: /erris.gov.ro/Center-of-Excellence-in-Derm).

Carol Davila University of Medicine and Pharmacy (UMFB) is the oldest medical and pharmacy university in the country with a rich research tradition. Between 2011-2016, 4096 articles were published (21123 citations) and 18 POSDRU programs were carried out. In 2016, 80 research projects were carried out (12 international, 68 PNII and PNIII). The Center for Research in Dermatology has a modern material base and has developed structural projects: capacity 334/2007 Research base [...] in dermatology; POSDRU 31081 Development of dermato-oncology [...]; POSCCE 512/323/2011 Educational portal [...] in dermato-oncology. Other research projects in dermato-oncology: PN-II-RU-TE-2011-3-0249, PNII.41-083 / 2007, CEEX.18 / 2005, PNII.62074 / 2008. The team involved published 10 ISI indexed articles in the field (5 in IF> 2) in 2016-2017, in collaboration with CO and P2, and has a national patent in dermatology. The members of the team are experienced researchers (CIS, professor, professor, chief of works) and doctoral students with project themes. The Infrastructure of the Center for the Excellence in Dermatology of the UMFB includes a skin imaging laboratory with a confocal microscope in vivo (fixed and portable) and ex vivo, digital dermoscope Fotofinder, dermatological surgery room (https://erris.gov.ro/CENTRE-OF-EXCELLENCE-IN-DERM). The Department of Pathology of UMFB's Dental Facility has equipment used in the teaching process at bachelor's, doctoral and postgraduate level (https://erris.gov.ro/Discipline-of-Pathology); UMFB is a partner in PATHUNIT and PATHOPLUS (see SCC infrastructure).

Components Projects

P1 Genomic / Proteomic Approach to Improve Diagnosis / Prognosis in Basal Cell and Squamous Cell Carcinoma

Non-melanomatous skin cancer is the most common form of cutaneous malignancy with an alarming increase of incidence, mainly due to cumulative exposure to solar radiation. The most common types are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), tumors of different pathobiological, phenotype and clinical behavior. From a histopathological point of view, SCC and BCC have different immunohistochemical profiles. Thus, BCC is 100% positive for Bcl-2, 75.8%, positive for CD10 and negative for CEA and EMA, while in SCC Bcl-2 expression is limited (under 5% of cases), CEA is positive in 34.5% of cases, EMA positive in 82.7% of cases and CD10 negative. Although from a morphopathological and immunohistochemical point of view SCC and BCC are different entities, cases of basquoquamous carcinomas are described, some being BCC with squamous cell differentiation in tumor structures, other true BCC-SCC colision tumors; Diagnosis can also be difficult in case of differentiation from non-invasive precursor lesions (actinic keratosis, Bowen's disease) or benign proliferations such as seborrheic keratosis; moreover, both SCC and BCC with the same morphopathological or classical immunophenotypic characteristics have different biological evolution, frequent relapses with aesthetically and functionally devastating consequences and / or the occurrence of metastases. Thus, the scientific novelty of this project is the investigation in correlation with standard IHC markers of protein expression involved in intercellular interactions, tumorigenesis, cell cycle regulation and apoptosis. Correlation of new markers investigated with standard markers will lead to the development of a complex IHC marker panel that will improve diagnosis in SCC and BCC.

Investigating the expression of these proteins compared to control samples (normal tissue, seborrheic keratosis, actinic keratosis) will result in a set of clear differentiation markers between benign or precancerous tumor pathologies (i.e. actinic keratosis) and non-melanomatous SCC and BCC tumor types. The scientific novelty of this project also resides in the correlation for the first time at the tissue level of the new proteins investigated with genes of interest in SCC and BCC as a way to improve prediction of the prognosis of these non-melanomatous tumors.

P2. Identifying a tissue pattern to improve prognosis in melanoma

Skin melanoma is the most aggressive type of skin cancer; its incidence is steadily increasing especially among the active population, and the death rate due to metastasis is extremely high despite new immune therapies or BRAF kinase inhibitor therapies approved in recent years. The molecular particularities of the different stages of diagnosis and the personalization of immuno-therapy are the major desires of clinical management of the patient with melanoma. The low rate of success of anti-melanoma therapies is also motivated by the fact that the molecular mechanisms and pathways that operate in the metastatic progression and the therapeutic resistance of this neoplasm are far from being elucidated. The complexity of this skin tumor involves a number of medical specialties such as dermatologist, pathologist, plastic surgeon, and last but not least the oncologist. In addition, the field of research can bring new information on the molecular details of tumorigenesis pathways and metastasis so that the approach to this pathology has to be done in a multi-, inter- and trans-disciplinary manner. The scientific novelty of the proposal follows two directions: the detection of intimate molecular mechanisms of tumorigenesis with identification of new therapeutic and translational targets by the development of validated sets of markers for melanoma patient management. This will be the first time to investigate the immune / tissue pattern in correlation with the circulating immune pattern for detecting the marker set that improves the

diagnosis, guides the immune / therapy and brings new data on prognosis into cutaneous melanoma. Given that Nivolumab immuno-therapy has recently been nationally approved (16 May 2017), we propose for the first time at national level to investigate the circulatory immune pattern of patients diagnosed with melanoma undergoing this innovative therapy, immune markers that can identify the effectiveness of therapy. Another novelty is to investigate the potential of new CRISPR / Cas9 molecular technology to study the dynamics of melanoma signaling molecular networks focusing on the Dopachrom tautomerase (DCT) gene, the gene involved in melanogenesis.

P3. Methodological principles of therapy orientation in dermato-oncology

The therapeutic principles for BCC and SCC are closely related to the degree of recurrence or metastasis; the metastatic potential implies a gloomy prognosis and involves adjunctive therapy (radiotherapy, chemotherapy), targeted therapy or immunotherapy. About 90% of SCC and 60% of BCC show an overexpression of EGFR that is associated with a bad prognosis, and the degree of expression of EGFR generally correlates with response to therapy. Blocking EGFR with specific molecules may be a therapeutic option in these tumor types; gefitinib and panitumumab are EGFR inhibitors with rather promising activity. Recent studies also indicate the alteration of the HH pathway in CAB, and future therapeutic options tend to associate HH inhibitors with EGFR inhibitors. The combination of inhibitors (targeted therapy) and adjuvant therapies is a future approach to the treatment of advanced forms of non-melanoma tumors. Reducing cutaneous toxicity that may occur in combination therapy is a multidisciplinary challenge that can contribute to side-effects and early detection. In vitro studies on the toxicity of new therapeutic principles are typically performed by end-point methods, fixed cell function evaluations. The novelty of the proposed project is to establish principles for evaluation methods of therapeutic agents, including real-time cellular monitoring over several days, providing exhaustive experimental data. These methods do not exclude end-point cytotoxicity determinations, having the capacity to be self-supporting and complementary. In addition, the proposed methodologies include real-time imaging of a scratch-curing, which is valuable in the context of skin toxicity, which may appear as a side effect in the combination of EGFR / HH blockade. Animal models of cutaneous carcinogenesis and incision-cutaneous excision as well as microchiral approaches complement the panel of methodologies for testing new therapies / therapeutic compounds.

P4. Bio-medical training in dermato-onco / pathology for doctors and young researchers

Skin cancers are by far the most common forms of cancer, even though they are often underdiagnosed or ignored by both the patient and the physician, probably due to the low morbidity and mortality of some skin cancers (carcinoma basal cellular). However, these characteristics can not be under any circumstances extrapolated for dermato-oncology as a whole, given the extreme aggressiveness of other forms of skin cancer such as melanoma or Merkel cell carcinoma.

Non-melanomatous skin cancers (mainly basal cell carcinoma and squamous cell carcinoma -) are currently the most common types of cancers in the Caucasian population, representing for example more than one-third of adult cancers in the United States 18-20 times more than cases of melanoma. Their incidence has steadily increased throughout the world over the last four decades; in Europe their incidence is estimated at 0.12%. Melanoma (MM) is one of the most aggressive tumors in all oncology, with increasing incidence, morbidity and high mortality, affecting the young population and involving considerable treatment costs. It accounts for 2-7% of skin cancers, with a rising incidence. Early diagnosis of MM as well as the establishment of prognostic tissues and blood indices is of major importance for increasing life expectancy, but also for reducing the cost of medical care. The diagnostic

approach to many skin conditions, especially skin cancers, currently depends on histopathological analysis of excised and processed tissues. The recent development of imaging techniques provides in vivo skin viewing, non-invasive and high resolution, thus overcoming the drawbacks of biopsy and histopathological analysis. These techniques include dermatoscopy, reflective confocal microscopy, high frequency ultrasonography, optical coherence tomography and magnetic resonance imaging. Treatment of skin cancers can be done both by modern non-invasive (eg photodynamic therapy) and invasive, the gold standard being MOHS surgery, which ensures maximum tissue preservation. These diagnostic and treatment methods are not addressed (as it results from consultation with the scientific secretariats of the partner universities) in any of the partner country medicine universities at the level of bachelor and master studies. Moreover, radiotherapy (one of the classical methods of treatment) is not studied at all or extremely stunning information is given during the dermatology stage; in the case of chemotherapy, it is studied at oncology trainees where none of the partner institutions treats skin cancers.

As such it can be said that the Romanian medical higher education does not currently prepare specialists who can professionally approach these extremely frequent diseases with extremely high mortality and morbidity and discover serious loopholes in the general medical culture of all graduates.

Dermatopathology (DP) provides the histopathological diagnosis of skin conditions, requiring etailed knowledge in dermatovenerology (DV) and pathology anatomy. The difficulty in acquiring the knowledge required to practice DP is recognized worldwide, DP being a recognized medical competence in the EU and the US with training curricula and professional level examinations (http://www.icdermpath.org/1/). Currently in Romania there is no DP competence. The AP and DV curricula in the Bachelor's degree studies touch upon some DP problems; there are no masters studies in the field; Residency curricula in pathology and DV include short DP modules (3 months for AP, 2 months for DV), absolutely insufficient. For prospective dermatologists, the lack of general pathological knowledge makes the level of information gained in the DP stage insufficient for understanding a histopathological bulletin of a skin condition and hinders collaboration with the anatomopathologist; for future pathologists (who subsequently will diagnosed DP), the lack of DV clinical knowledge and the short study time allow only superficial orientation in the field, the specialization itself being to be done at the work place being the strike of an inevitable learning curve with errors materialized in substandard medical services provided to those patients.

Disemination of the results of the research. Stage 1 2018

A. articles in extenso:

1. Variation in expression of inflammation-related signaling molecules with profibrotic and antifibrotic effects in cutaneous and oral mucosa scars. Bucur M, Dinca O, Vladan C, Popp C, Nichita L, Cioplea M, Stinga P, Mustatea P, Zurac S, Ionescu E. Journal of Immunology Research, Vol. 2018, Article ID 5196023, ISI
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10. In vivo Confocal Laser Scanning Microscopy Imaging of Skin Inflammation: Clinical Applications and Research Directions. Ilie (Ghita) MA, Caruntu C, Lixandru D, Tampa M, Georgescu S, Constantin MM, Constantin C, Neagu M, Zurac S, Boda D. Experimental and Therapeutic Medicine. 2018. ISI.
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12. The Central Role of Inflammation Associated with Checkpoint Inhibitor Treatments. Vajaitu C, Draghici C, Solomon I, Lisievici C, Popa A, Lupu M, Caruntu C, Constantin M, Voiculescu V. Journal of Immunology Research. 2018.ISI
13. New Insights in the Pathogenesis of HPV Infection and the Associated Carcinogenic Processes: The Role of Chronic Inflammation and Oxidative Stress. Georgescu S, Mitran C, Mitran M, Caruntu C, Sarbu M, Matei C, Nicolae I, Tocut S, Popa M, Tampa M. Journal of Immunology Research. 2018. ISI
14. Unveiling Ga (III) phthalocyanine – a different photosensitizer in neuroblastoma cellular model. Constantin C, Lupu A, Fertig T, Gherghiceanu M, Pop S, Ion R, Neagu M. Journal of cellular and molecular medicine. 2018. ISI
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B. posters and oral presentations presented at national, european or international congresses / conferences:

1. Malignant blue melanoma: an institution experience in 4 cases. Stinga P, Popp C, Cioplea M, Cioroianu A, Dutulescu S, Andrei R, Dumitru C, Chitu V, Boda D, Caruntu C, Zurac S. 30th European Congress of Pathology / Virchows Archiv (2018) 473 (Suppl 1):S1–S340. Sept. 2018. Poster

2. Cellular dermatofibroma – a challenging diagnosis. Vrancianu A, Costache D, Bulf R, Zurac S, Andrei R. 30th European Congress of Pathology/Virchows Archiv(2018)473(Suppl 1):S1–S340.Sept. 2018. Poster
3. A rare case of synchronous chronic lymphocytic leukemia/small cell lymphocytic lymphoma and metastatic clear cell variant of cutaneous squamos cell carcinoma in cervical lymph nodes. Stinga P, Cioroianu A, Popp C, Cioplea M, Barbuceanu O, Zurac S. 30th European Congress of Pathology/Virchows Archiv(2018)473(Suppl 1):S1–S340.Sept. 2018. Poster
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10. Genomic copy number variants in regressed areas of cutaneous melanoma - array-based comparative genomic hybridization analysis. Neagu M, Constantin C, Zurac S. EADO 2018 Congress Abstracts Nov. 2018. Poster
11. Lymphocytes subsets in murine cutaneous melanoma model -– potential biomarkers for therapy monitoring. Isvoranu Gh, Constantin C, Surcel M, Huica R, Munteanu A, Neagu M, Ursaciuc C, Zurac S. EADO 2018 Congress Abstract. Nov 2018. Poster
12. Omics Perspectives in cutaneous melanoma: current instruments in management of the pathology. Constantin C, Neagu M, Zurac S. Second National Congress of Immuno-Dermatology Association with International participation. Sept. 2018. Prezentare orală
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