Prof. Edoardo Alesse ***Research Project Title:*** Novel approaches for the characterization and modulation of the oncogenic Sonic Hedgehog pathway in colorectal cancer. Identification of new potential prognostic markers and therapeutic targets. ***PI:*** Enrico De Smaele (University of "Sapienza", Rome) ***Other Research Units:*** Edoardo Alesse, Chiara Compagnoni (University of L'Aquila).	***ERC Field:*** LS – Life Sciences ***BREEF PROJECT DESCRIPTION:*** The project aims at deepening the molecular mechanisms of colorectal tumorigenesis with reference to the Sonic Hedgehog pathway. The study will be focused on the molecular characterization of specific carcinogenesis mouse models, and to the analysis of miRNAs targeting KCASH2 in in vitro and in vivo models as well as colorectal cancer patients, with the purpose to identify new candidate biomarkers and therapeutic targets. **Kwords:** Hedgehog pathway, KCASH2/KCTD21, colorectal cancer, miRNA, therapeutic approaches, animal models

Prof.ssa Daria Capece ***Research Project Title:*** Targeting cancer stem cell (CSC) metabolism by exploiting ncRNAs to improve drug therapy outcome in lung cancer ***PI:*** Joanna Kopecka (University of Torino) ***Other Research Units:*** Daria Capece, Monica di Padova (University of L'Aquila); Ilaria Dando (University of Verona); Silvia Zappavigna (University of Campania "Luigi Vanvitelli").	***ERC Field:*** LS – Life Sciences ***BREEF PROJECT DESCRIPTION:*** The aim of this project is to identify those non coding RNAs (ncRNAs) that regulate CSCs metabolism as potential targets that will be hit to eradicate this aggressive cancer subpopulation in the context of lung cancer. Over the past two decades, there has been a tremendous shift in cancer treatment, from broad-spectrum cytotoxic drugs to target therapy and immunotherapy. Therefore, the identification of specific CSC-related ncRNAs could represent a definitive turning point for the eradication of this aggressive subpopulation within the tumor, thus decreasing the appearance of relapses, which are strictly linked to the presence of CSCs. **Kwords:** CSCs; ncRNA, metabolism, lung cancer

Prof. Pierangelo Cifelli	***ERC Field:*** LS4-Physiology in Health Disease and Ageing
Research Project Title: Neurosteroids as Determinants of Seizure Susceptibility to Stress ***PI:*** Giuseppe Biagini (University of Modena e Reggio Emilia) ***Other Research Units:*** Pierangelo Cifelli (University of L'Aquila); Antonio Torsello, (University of Milano Bicocca).	***BREEF PROJECT DESCRIPTION:*** Stress has been proposed to play a critical role in the onset of epilepsy and can lead to a more severe disease phenotype when epilepsy is established. It is also reported that a stressful life is associated with and possibly responsible for depression and anxiety, which are common comorbidities of epilepsy. If there could be a link among stress, the burden represented by uncontrolled seizure recurrence, and epilepsy comorbidities such as depression, it is still undetermined. Interestingly, neurosteroids (NSs) are a family of diverse molecules directly synthesized in the nervous system, or obtained by processing the circulating steroids after their passage through the blood-brain barrier, which potently reduce anxiety, exert an antidepressant action, and antagonize seizures by stimulating the gamma-aminobutyric acid type A receptor (GABAAR). Specifically, in this proposal we hypothesize that stress could reduce the efficiency of NSs as an endogenous protective mechanism able to promote resilience to epileptic activity and mood disorders. We propose to investigate: (i) the role of stress in determining the onset of epilepsy and in promoting an increase in seizure frequency in epileptic rats; (ii) the reduction in NS availability in brain regions including the hippocampus and neocortex as possible explanation of the stress effects; (ii) preservation of the capability to modulate the GABAAR activity by NSs during the epileptogenesis and also in rats with spontaneous recurrent seizures; (iii) the beneficial effects of increasing brain NS levels by administering the 3beta-hydroxysteroid dehydrogenase/delta5-4 isomerase inhibitor trilostane; (iv) which specific NS could be responsible for the modulation of inflammation.
	Kwords: Epilepsy, Stress, GABA A receptors

Prof.ssa Paola Cipriani	***ERC Field:*** LS6_4 Malattie del Sistema immunitario; LS4_9 Metabolismo e disordini metabolici incluso diabete e obesità.
Research Project Title: The identification of common genetic, molecular, and cellular pathogenic mechanisms in diabetes and rheumatoid arthritis may shed new light in the development of a metabolic disease during a chronic inflammatory process and may identify new specific targets to derive a precision medicine driven therapeutic strategy ***PI:*** Roberto Giacomelli (Università Campus Biomedico Roma) ***Other Research Units:*** Paola Cipriani (University of L'Aquila); Annamaria Iagnocco (University of Torino).	***Breef Project Description:*** Rheumatoid arthritis (RA) is associated with changes in metabolism leading to insulin resistance (IR) and type II diabetes (T2D) due to glucocorticoid therapy, obesity, lifestyle factors. Proinflammatory cytokines. play a crucial role in the pathogenesis of both the diseases. We will evaluate the inflammatory cytokines signatures and genomic patterns in RA patients and comorbid T2D in comparison with patients with RA without comorbid and patients with T2D only. We will explore immune modulating features of GLP1 agonists on key cells involved in RA-T2D axis. Moreover, we plan compare synovial features among T2D and RA patients based on genomic, histologic, and ultrasound evaluations. On this basis, the study of mechanisms involved in both the diseases is mandatory to identify new molecular targets allowing clinicians to use a single treatment controlling both these diseases. On these bases, the identification of common genetic, molecular, and cellular pathogenic mechanisms in diabetes and rheumatoid arthritis may shed new light in the development of a metabolic disease during a chronic inflammatory process and may identify new specific targets to derive a precision medicine driven therapeutic strategy.
	Kwords: autoimmune diseases, rheumatoid arthritis, type 2 diabetes, precision medicine, latent autoimmune diabetes in adults (LADA), inflammation

Prof.ssa Simonetta D'Amico ***Research Project Title:*** PAROLA Parenting APP for promoting language acquisition ***PI:*** Annalisa Guarini (Università di Bologna) ***Other Research Units:*** Simonetta D'Amico (University of L'Aquila); Maja Roch (University of Padova).	***ERC Field:*** SH4 The Human Mind and Its Complexity
	BREEF PROJECT DESCRIPTION: Language development is characterized by wide interindividual variability between 24 and 36 months, and some children show late language emergence with cascading effects at preschool and school age. Parents can mitigate the risk of language delay and proactively facilitate an optimal communication environment for their children. Recent studies have proposed that APPs can support parents of children with atypical development. The current project aims at developing the PAROLA APP for parents of children within the critical period between 24 and 36 months. The APP has two main goals: (1) collect data using an innovative *Ecological Momentary Assessment*, investigate the prevalence of linguistic delays in three Regions of North and South Italy, explore the association with risk and protective factors, describe linguistic profiles, support parents in observing their child's language development and referring possible difficulties to pediatricians and educators and teachers; (2) offer an *Ecological Momentary Intervention* to support parents in promoting their child's language acquisition through activities provided in the APP. The activities will promote language development components, integrating music, and book-sharing. The main hypothesis is that the PAROLA APP will improve a child's language development, thanks to an indirect effect mediated by parents.
	Kwords: Child Language; APP; Parenting; Dialogic book-sharing; Educational poverty; Late talkers

Prof.ssa Aurora D'Atri ***Research Project Title:*** How Emotional Reactivity and Memory Evolve over Sleep: psychophysiological Description via Exogenous manipUlation of Sleep features (HERMES-DEUS) ***PI:*** Nicola Cellini (University of Padova), ***Other Research Units:*** Aurora D'Atri, Daniela Tempesta (University of L'Aquila).	***ERC Field:*** SH4 The Human Mind and Its Complexity ***BREEF PROJECT DESCRIPTION:*** Emotional events have a favored status in memory. The emotions we experience every day constantly bias how we learn (encoding), what we remember (consolidation), and how we respond to these events. However, what we remember but also how we remember emotional events over time do not depend only on how we have encoded these events but also on how we consolidate them during sleep. REM sleep seems to play a key role in emotional memory processing, although several questions are still open. The project will address the role of REM sleep in diurnal emotional experience by combining behavioral and psychophysiological techniques with research designs aimed at: a) manipulating the quality and quantity of NREM/REM sleep through tactile stimulation during nocturnal sleep, b) manipulating the presence/absence of REM sleep, capitalizing on the physiology of daytime naps and circadian rhythms, and c) correlating sleep architecture over several nights with changes in emotional processing across days. Our project will provide strong experimental evidence about the effects of REM sleep on emotional processing (reactivity and memory) after a single sleep episode (nocturnal or daytime nap) and over several days. It will also provide data on the potential interplay between NREM and REM sleep in emotional processing. **Kwords:** Emotion, Memory, Psychophysiology, Sleep, Stimulation, REM

Prof.ssa Simona Delle Monache ***Research Project Title:*** Effect of Heat-not-burn tobacco (IQOS) versus Electronic and Tobacco cigarettes on the oral health: a multidisciplinary approach for a potential prevention strategy ***PI:*** Migliorati Graziella (University of Perugia) ***Other Research Units:*** Delle Monache Simona, Pulcini Fanny (University of L'Aquila); Scardina Giuseppe Alessandro (University of Palermo).	***ERC Field:*** LS3 Cellular, Developmental and Regenerative Biology ***BREEF PROJECT DESCRIPTION:*** In recent years, the "heat-not-burn" systems, including IQOS, have grown in popularity as a healthier alternative to traditional cigarettes (TS). With the increasing diffusion of electronic cigarettes (e-cig) and the growing consumer discontent due to the absence, or decrease, of the so-called "throat hit" associated with e-cig use, the "heat-not-burn" devices are gaining market shares. As such, their impact on human health is widely discussed among scientists, leading however to controversial and inconclusive results, thus boosting research to further investigation. In particular, their long-term biological and immunological effects are poorly known, especially in the oral cavity, the first target of exposure. The aim of this project is to compare the biological effects of IQOS with those of TS and e-cig in oral mucosa experimental models, including dental pulp stem cells (DPSCs), during the switching to dentin-pulp-like organoids, human biological samples (gingival biopsies, saliva and blood) and ex-vivo samples in order to extend the in vitro findings to a human setting, thus providing to the research a translational value and clinical importance. **Kwords:** toxicology, immunology, inflammation, stem cell biology,3D cell culture, chemical composition

Prof.ssa Maria Concetta Fargnoli ***Research Project Title:*** Cutaneous squamous cell carcinoma: stratifying high risk tumors with novel technologies **PI:** Caterina Longo (University of di Modena e Reggio Emilia) ***Other Research Units:*** Maria Concetta Fargnoli, Cristina Pellegrini, Dott. Marco Clementi (University of L'Aquila); Ketty Peris (Università Cattolica del Sacro Cuore, Roma); Elvira Moscarella (University of Campania "Luigi Vanvitelli")	**ERC Field:** LS - Life Sciences (LS4 Physiology in Health, Disease and Ageing) ***BREEF PROJECT DESCRIPTION:*** Cutaneous squamous cell carcinoma (cSCC) is the second most frequent epithelial skin cancer among Caucasians. Several clinical and histologic criteria have been defined for aggressive cSCC, however there is no consensus on which features better characterize the aggressiveness and predict tumor progression. The knowledge of deregulated molecular pathway associated with the risk of metastatic cSCC could help in clarifyng the potential aggressiveness, but an integrated clinical and molecular profile is lacking for this tumor. Our project aims to define a multidimensional molecular profile of aggressive cSCC by integrating clinical and molecular approaches. It consists of a discovery and a validation phase. In the discovery phase, we aim to define whether high risk cSCC hold a peculiar molecular signature compared to low risk cSCC by using high throughput molecular analysis (transcriptome, mutational profiling, immune-microenvironment profiling). In the validation phase, the identified molecular alterations of aggressive cSCC will be tested on a prospective cohort by using immunohistochemistry, and DNA target-sequencing analysis on tumor tissues and liquid biopsy. All molecular data will be correlated with patients' and tumors' characteristics. **Kwords:** Skin cancer; squamous cell carcinoma; metastatic disease; genetic profiling; molecular genetics; biological bases of cancer

Prof.ssa Rita Maccarone ***Research Project Title:*** An innovative cross-species transcriptome approach to target retinal cell dysfunction in age-related macular degeneration. **PI:** Rita Maccarone, (University of L'Aquila) **Other Research Units:** Rita Maccarone, Flati Vincenzo, Zerti Darin, Carozza Giulia (University of L'Aquila); Lucia Poggi (University of Trento); D'Angelo Rosalia (University of Messina).	**ERC Field:** LS5 Neuroscience and Disorders of the Nervous System ***BREEF PROJECT DESCRIPTION:*** The degeneration of retinal pigmented epithelial cells RPE is one of the main events that induces vision loss in Age related Macular degeneration (AMD), the leading cause of blindness in the worldwide. It is well known that non-coding RNAs (microRNAs, circular RNAs and long non-coding RNAs), play a crucial role in the etiology of retinal degeneration. The aim is to perform a cross-species transcriptome analysis thanks of a multidisciplinary team with complementary long-standing expertise in ophthalmic research. **Kwords:** Age related Macular Degeneration; zebrafish regeneration; retina protection;oxidative stress; trascriptomic; nanomedicin

Prof. Mauro Maccarrone ***Research Project Title:*** Intersection between endocannabinoid signalling and resolution of inflammation in Alzheimer's disease **PI:** Mauro Maccarrone, University of di L'Aquila **Other Research Units:** Mauro Maccarrone Francesca Pistoia, Aldo Giovannelli, Lucia Scipioni, Dr. Roberto Coccurello (University of L'Aquila); Sergio Oddi, Cinzia Rapino, Roberto Giacomelli-Stuffler, Ana Lia Bernardi Leonardi, Eleonora Oliva, Francesca Ciaramellano (University of Teramo).	**ERC Field**: LS - Life Sciences / LS1_2 Biochemistry ***BREEF PROJECT DESCRIPTION:*** In-between the acute inflammatory response and escalation of Alzheimer's disease neuropathology, there is a phase of homeostatic balance and possible removal of phlogistic source, where inflammatory cascade and tissue damage can (or can not) be resolved. During this "resolution of inflammation", several processes are orchestrated by specific lipid signals, known as specialized pro-resolving mediators. Here, we aim at interrogating their possible cross-talk with additional bioactive lipids called "endocannabinoids". **Kwords:** Endocannabinoids, Immunochemistry, Resolution of inflammation, Signal transduction

Prof.ssa Mazza Monica **Research Project Title: F**eel good! Social robot-mediated video modeling intervention to facilitate communication between healthcare professional and patient with autism spectrum disorder **PI:** Mazza Monica (University of L'Aquila) **Unità di ricerca:** Monica Mazza, Marco Valenti, Di Giovanni Chiara, Tepidino Michele, Sabetti Lelio (University of L'Aquila); Gena Cristina (University of Torino); De Carolis Berardina (University of Bari).	***ERC Field:*** SH3- Social Science and Humanities **BREEF PROJECT DESCRIPTION:** Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by absent or impaired verbal communication. Video modelling (VM) is an effective practice in ASD based on teaching a wide range of social and everyday skills through video observation. This study proposes the Ministero dell'Università e della Ricerca MUR - BANDO 2022 realization of an intervention that aims to integrate these technologies to encourage, in people with ASD, the development of communicative ability, better interaction and compliance with the clinician and expression of their discomfort, during the clinical visit. THis approach allows for ongoing training both in specialized centres, which do not have the robot, and at home, allowing parents to follow their children in the family context. This will be possible thanks to the personalization and adaptation of the intervention according to the severity of the ASD person. To ensure the correct degree of personalization, the VM technique will involve the creation of peer modelling and prompting modelling videos that consider the specific life situations, social context and characteristics of the person. The design of serious games that integrate VM will follow a user-cantered approach. **Kwords:** Autism Spectrum Disoeder, Health prevention ,Intervention Video-Modeling . Social Robot. Serius Games

Prof. Luciano Mutti	***ERC Field:*** LS6_4 Malattie del Sistema immunitario; LS4_9 Metabolismo e disordini metabolici incluso diabete e obesità.
Research Project Title: Molecular evaluation of the prognostic impact of BAP1 status in malignant pleural mesothelioma and renal cell carcinoma ***PI:*** Luciano Mutti, (University of L'Aquila) ***Other Research Units:*** Prof Camilo Porta. University of Bari	***BREEF PROJECT DESCRIPTION:*** Given the opposite clinical effect of BRCA Associated Protein gene (BAP1) status and the BAP1-regulated 1inositol-1,4,5-trisphosphate receptor 3 (IP3R3) function in Malignant Pleural Mesothelioma (MPM) and Renal Cell Carcinoma (RCC) will study their interaction and biological effects in both of these malignancies. BAP1 and IP3R3 will be modulated through gene knock-down or overexpression and the biological behavior of cells will be evaluated through proliferation, spheres/spheroids formations, cell death assays and apoptosis before and after oxidative stress Spheres/spheroids will be then characterized focusing on the expression of stemness markers . Moreover, their metabolism will be studied with sea-horse analysis and metabolomics together with the changes in RNA-seq analysis after gene silencing of BAP1 and/or IP3R3, Eventually we will focus on the role played by calcium cell fluxes and calcium machinery during spheres/spheroids formation and after pro-apoptotic stimulation. We expect to find possible calcium modulators both through docking analysis of the IP3R3 receptor with particular attention to Ca++influx from ER to mitochondria and selecting already known possible modulators of the calcium machinery
	Kwords: BAP1; Mesothelioma; Renal Cell Carcinoma

Prof. Mariagrazia Perilli ***Research Project Title:*** Fighting Carbapenemases Resistance by Kinetic Guided Target Synthesis (CARESS) ***PI:*** Mariagrazia Perilli (University of L'Aquila) ***Unità di ricerca:*** Mariagrazia Perilli (University of L'Aquila); Emilia Caselli (University of Modena-Reggio Emilia); Gian Maria Rossolini (University of Firenze).	**ERC Field:** LS6_9 LS6_9 Antimicrobials, antimicrobial resistance. **BREEF PROJECT DESCRIPTION:** CARESS aims to use a Kinetic Target-Guided Synthesis (KTGS) as a powerful strategy to discover new MBL inhibitors. In KTGS the biological target (e.g. an enzyme) selects its own inhibitors by assembling them from building blocks in a biocompatible reaction. In particular, the inhibitors are formed in situ via an irreversible process once the building blocks are bound to adjacent pockets of the target in the proper orientation and in close proximity. Most ligands used in KTGS are conform with "possible to be oral chemical space" properties that facilitate the investigation of a broader chemical space and allow a quick and efficient screening of several small-molecules, thus expediting the process of hit identification. The usefulness of KTGS in drug discovery has been established in several therapeutic areas and with over 25 targets reported. Among different biomolecules targeted, KTGS has been preferentially applied to enzymes. Although, KTGS has been successfully used with a plethora of chemical transformations, the vast majority of experiments reported involves the formations of triazoles starting from biocompatible alkynes and azides. **Kwords:** Beta-lattamasi, Inibitori, KTGS

Prof. Piero Ruscitti ***Research Project Title:*** The PIANO project, Pathways Involved in the action of ANti-MDA5 antibodies: impact On innate immunity ***PI:*** Ruscitti Piero (University of L'Aquila) ***Other Research Units:*** NavarinI Luca (Università "Campus Bio-Medico" Roma); Cavagna Lorenzo (University of Pavia)	***ERC Field:*** LS- Scienze della vita ***BREEF PROJECT DESCRIPTION:*** Melanoma Differentiation Antigen 5 (MDA5) is a cytosolic intracellular pattern recognition receptor involved in the innate immunity towards viruses, recognizing long double stranded RNA (dsRNA) and activating type I interferon and NF-KB pathways. Anti-MDA5 antibodies are markers of a specific myositis subset that may present with an often refractory and fatal lung manifestation (Rapidly Progressive Interstitial Lung Disease, RP-ILD). RP-ILD is characterized by hyperferritinemia and by an aberrant activation of type I interferon and NF-KB pathways. As not all patients develop RP-ILD, the pathogenic role of anti-MDA5 antibodies (as a whole and of their single specificities) and of ferritin needs to be defined. In fact, ferritin may be part of the mediators of inflammation in RP-ILD. The project addresses the function of single anti-MDA5 antibody specificities targeted onto MDA5 epitopes and of ferritin in different in vitro models, focusing on the effect on type I interferons and NF-KB pathways. The working hypothesis is that anti-MDA5 antibodies and hyperferritinemia stimulate type I interferon and NF-KB pathways by activating MDA5, possibly triggering a ferritin-based inflammation loop. With this project, we will clarify the action of anti-MDA5 antibodies and ferritin on MDA5 activity, providing a general approach adaptable to pathogenic studies of similar conditions and identifying possible disease biomarkers/diagnostic kit and targets for therapy. **Kwords:** -anti-MDA5 antibodies -rapid progressive interstitial lung disease -ferritin -Type I interferons -NF-KB pathway

Prof.ssa Simona SACCO ***Research Project Title:*** Exploring the effects of lamotrigine on interictal neurovascular coupling within visual network in patients with migraine with aura: a multiparametric longitudinal study with EEG-fMRI and multi-delay 3D-pseudocontinous arterial spin labeling. **PI:** Antonio Russo (University of Campania "Luigi Vanvitelli") **Other Research Units:** Simona Sacco, (University of L'Aquila)	***ERC Field:*** LS- Scienze della vita ***BREEF PROJECT DESCRIPTION:*** Migraine is a common neurological disorder characterized by recurrent headaches accompanied by various non-pain symptoms. Some patients experience a reversible focal neurological phenomenon called migraine aura, which involves gradual spreading and disappearance of symptoms. Advanced neuroimaging studies have revealed abnormalities in the extrastriate cortex, a part of the visual network, considered the "aura generator." Although previous studies have explored brain function and blood flow changes separately, there has been no investigation using simultaneous functional MRI-EEG (fMRI-EEG) acquisition, which could provide a more comprehensive understanding of the condition. The project aims to explore the pathophysiology of migraine aura by studying brain function and local perfusion using longitudinal simultaneous EEG-fMRI and multi-delay 3D pseudo-continuous arterial spin labeling-MRI techniques. The researchers hypothesize that patients with migraine aura may have dysfunctional neurovascular coupling, possibly playing a crucial role in triggering the aura phenomenon. The study will focus on the interictal period, the time between migraine attacks, to analyze abnormal neurovascular coupling in the visual network's strategic areas. The study will involve comparing patients with migraine aura, patients with migraine without aura, and a group of healthy controls of similar age and sex to identify distinctive neuroimaging features and provide insights into the pathophysiology of migraine aura. **Kwords**: Migraine with aura, Neurovascular coupling, Neuroimaging, Functional connectivity, Arterial spin labeling, Visual network