SCIENTIFIC COMMUNICATIONS

1

TDP-43 cytoplasmic inclusions in the skin of ALS patients. Miguel A. Rubio[1, 2], Mireia Herrando-Grabulosa[2], Roser Velasco[2,3], Israel Blasco[2], Monica Povedano[4], Xavier Navarro[2] 1 Neuromuscular Unit, Department of Neurology, Hospital del Mar, Barcelona, Spain. 2 Department of Cell Biology, Physiology and Immunology, Institute of Neurosciences and CIBERNED, Universitat Autònoma de Barcelona, Bellaterra, Spain. 3 Neuro-Oncology Unit, Department of Neurology, Hospital Universitari de Bellvitge-ICO and IDIBELL, L'Hospitalet, Spain. 4. Department of Neurology, Hospital Universitari de Bellvitge, L'Hospitalet, Spain. Unidad de Neuromuscular, Servicio de Neurología, Hospital del Mar, Barcelona, España. 2 Departamento de Biologia Celular, Fisiología e Inmunología, Instituto de Neurociencias y CIBERNED, Universitat Autònoma de Barcelona, Bellaterra, España

Key words: amyotrophic lateral sclerosis, dermis, skin biopsy, TDP-43, biomarker

ABSTRACT: Background. To identify and quantitatively analyze cytoplasmic TDP-43 inclusions in epidermis and dermis of the skin of ALS patients. Methods. Skin biopsies from 64 subjects were analyzed: 44 ALS patients, 10 healthy controls (HC) and 10 neurological controls (NC) (5 patients with Parkinson's disease and 5 with multiple sclerosis). TDP-43 immunoreactivity in the epidermis and dermis was analyzed, as well as the percentage of cells with TDP-43 cytoplasmic inclusions in predefined areas of epidermis and dermis (papillary and reticular). ROC analyses of these data were also performed. A subset of ALS patients was again biopsied 12 months later for comparison over time. Results. We detected higher expression of TDP-43 in the epidermis ($p<0.001$) and in both layers of the dermis ($p<0.001$), as well as higher percentage of TDP-43 cytoplasmic positive cells ($p<0.001$) in the ALS group compared to HC and NC groups. Dermal cells containing TDP-43 were fibroblasts as identified by co-labelling against vimentin. ROC analyses (AUC 0.867, $p<0.001$; CI 95% 0.800-0.935) showed that detection of 24.1% of cells with cytoplasmic TDP-43 positivity in the dermis had 85% sensitivity and 80% specificity for detecting ALS. We did not find significant correlation with clinical features, including disease onset and ALSFR-R slope. Conclusions. In this study we have identified significantly increased TDP-43 expression in the epidermis and cytoplasmic aggregations of TDP-43 in the dermis of ALS patients. Our findings provide insight into the TDP-43 expression in non-neural tissue in ALS and support its use as a potential biomarker.

2

Validation of the ultrasonographic and manometric study of the tongue as indicators of bulbar involvement in patients with Amyotrophic Lateral Sclerosis (ALS). Bernat Bertran Recasens[1], Miguel Ángel Rubio Perez[1], Anna Guillen Sola[2]. 1. Unidad de Neuromuscular del Hospital del Mar de Barcelona. 2. Servicio de Medicina Física y Rehabilitación del Hospital del Mar de Barcelona

Keywords: dysphagia, tongue, tongue strength, tongue thickness, videofluoroscopy.

ABSTRACT: Introduction: A third of the ALS patients, in the beginning, and 85% throughout the disease, present bulbar dysfunction. Currently, there is no consensus on when and how dysphagia should be evaluated. Since the oral phase of swallowing is the first to be affected, and the tongue plays an important role, its study can be of great relevance for patients' follow-up. Objective: 1) To compare the quantitative value of the anterior and posterior lingual force (IOPI® system) and the lingual thickness (ultrasound) with the findings of the videofluoroscopy (VDF). 2) Correlate tongue strength and thickness with disease severity (ALSFRS-R scale). Results: 22 patients with ALS have been studied. A

correlation has been found between the lingual strength parameters and the ALSFRS-R scale (anterior: p = 0.007; posterior p= 0.009) and ALSFRS-R bulbar subscore (p<0.001; posterior p = 0.001), as well as the alterations qualitative results of the oral phase using VDF (previous: p = 0.05). There is no correlation between tongue thickness and the parameters studied. On the other hand, in the follow-up of the patients, it has been found that the tongue strength is a pre-clinical marker of bulbar dysfunction since it presents pathological values 3-6 months earlier than the ALSFRS-R bulbar subscore. Conclusions: The functional study of the tongue with the IOPI® system can be an easy to perform, reproducible and non-invasive tool that allows monitoring patients with ALS and selecting, without requiring a VDF, those who need an adaptation of diet and/or gastrostomy.

3

Nicotinamide riboside, pterostilbene and pde4 inhibitors in the treatment of ALS. Elena Obrador, Rosario Salvador-Palmer and José M. Estrela. Professors of Physiology, Faculty of Medicine, University of Valencia, 15 Av. Blasco Ibañez, 46010 Valencia, Spain.

Key words: ALS; NAD+; Pterostilbene; antioxidant defences; Sirtuins; neuroinflammation; Ibudilast.

ABSTRACT: Oral administration of nicotinamide riboside (NR, NAD+ precursor) and pterostilbene (PT, a natural antioxidant polyphenol) increase sirtuin activity, antioxidant defences, and mitochondrial function, exerting protective effects against neurodegeneration in vivo. We demonstrated the efficacy of dietary supplementation with EH301 (NR+PT) in a placebo-controlled double-blind pilot study in ALS patients. After 4 months, EH301-treated ALS patients showed significant improvements in the ALSFRS-R score, pulmonary function, muscular strength, skeletal muscle/fat weight ratio, and a slowdown in disease progression. In the clinical evaluation carried out one year later, these improvements still remained (de la Rubia et al., 2019). Neuroinflammation and oxidative stress pave the way leading to motor neuron death in ALS (Obrador et al. 2020). The levels of proinflammatory cytokines are increased in the CSF of SOD1G93A mice and humans with ALS. EH301 treatment decreases microgliosis, astrogliosis, oxidative stress, TNFα-induced cytotoxicity and loss of neuromotor functions associated with ALS progression, and significantly increases survival of SOD1G93A mice (Obrador et al., 2021). We are testing the advantages of combining EH301 with an anti-inflammatory drug, promising the results with Ibudilast, a phosphodiesterase-4 (PDE4) inhibitor, currently in clinical trials for the treatment of ALS in the USA. Compelling pre-clinical data of our laboratory show that EH301+Ibudilast increase mean survival of SOD1G93A mice (191 days) compared to controls or those treated with either EH301 or Ibudilast (133, 153, 137 days respectively) (P<0.01). These improvements were reproduced using FUSR521C mice. Our results demonstrate a synergistic interaction between EH301 and Ibudilast with potential therapeutic benefits against ALS.

4

Deciphering the role of neuroinflammation and the peripheral immune system in ALS Oriol Dols-Icardo Sant Pau Biomedical Research Institute Postdoctoral researcher.

ABSTRACT: Neuroinflammation is a pathological hallmark of amyotrophic lateral sclerosis (ALS). Through the combination of massive RNA sequencing, recently developed bioinformatic tools and immunohistochemistry applied in the motor cortex of ALS patients and healthy controls, we recently demonstrated that neuroinflammation is the most important event in this brain region and microglia play a major role in this process.

Furthermore, for the first time in the ALS motor cortex, we identified a microglial subpopulation (known as disease associated microglia (DAM)) which express high levels of major histocompatibility class II markers (MHCII), as the main driver of neuroinflammation, microgliosis, neurodegeneration and synaptic dysfunction (Dols-Icardo et al., Neurol. Neuroimmunol. Neuroinflamm. 2020). By the other hand, recent studies have shown that peripheral immune cells (PIC) present in the blood of patients with neurodegenerative diseases, including ALS, contribute to neuroinflammation and infiltrate in the central nervous system (CNS). Specifically, under neurodegenerative conditions, DAM interacts with PIC and promotes their infiltration in the CNS through MHCII. Our ongoing project is focused on the study of PIC in the blood of ALS patients and healthy controls using single-cell RNA sequencing. As the peripheral immune system is easily accessible, the ultimate goal of this project is to accelerate the development of novel peripheral biomarkers and therapeutic strategies for ALS, which might target neuroinflammation and modify the disease course. Keywords: amyotrophic lateral sclerosis, microglia, neuroinflammation, peripheral immune cells, biomarker, therapeutic target, single-cell RNA sequencing.

5

Identifying BMI-associated pathways that confer protection in ALS. Silvia Corrochano Sánchez. Fundación para la Investigación Biomédica del Hospital Clínico San Carlos, Madrid. KEYWORDS: genes, weight, Body Mass Index (BMI), protection, SOD1G93A, leptin. ABSTRACT: Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disorder for which there is currently no cure. ALS is a complex and multifactorial disease where genetic and environmental factors interact and contribute to its appearance, which suggests considering combined and personalized therapies. There is a strong positive association between body mass index (BMI) and survival in ALS, where patients with a higher BMI are more likely to show slower disease progression and longer survival; conversely, a low BMI is associated with accelerated disease progression. It is not known how a high BMI protects in ALS, so further research is needed to find an alternative to diet (or complementary therapy) and offer effective treatment to patients. The hypothesis in this study is that some genes involved in obesity or genes that cause alterations in lipid metabolism could, on the other hand, have protective effects on motor neurons, facilitating a metabolic adaptation that could prevent pathological states such as ALS. We use a classic transgenic mouse model, SOD1-G93A, and cross it with obese mice (mutants of the leptin gene). We conduct a study of differential gene expression in situations of disease and protection due to higher BMI in spinal cord and fat tissues. This allows us to study pathways or genes involved in protection and thus be able to study them as potential therapeutic targets.

6

Fine tunning a molecular diagnosis algorithm for patients with ALS and/or FTD Key words: diagnosis, genetic, algorithm, WES, NGS The progress in molecular diagnosis thanks to NGS development has led to an enormous increase in the genetic knowledge of ALS and FTD. Hernández D.1, Martín-Hordaza Ríos A.1, García-Escrihuela, O. 1, Cordero-Vázquez P.2, Herrero-Manso M.C.3, Villarejo-Galende A.4, Llamas-Velasco S.4, González-Sánchez M.4, Herrero-Sanmartín A.4, Expósito-Blázquez L.1, Martín-Casanueva M.A.5, Esteban-Pérez J.2 & García-Redondo A.1. 1-Grupo de Investigación en ELA. Instituto de Investigación Sanitaria Hospital 12 de Octubre, Madrid. 2-Departamento de Neurología – Unidad de ELA. Hospital

Universitario 12 de Octubre, Madrid. 3-Departamento de Reumatología - Hospital Universitario 12 de Octubre, Madrid. 4-Departamento de Neurología – Unidad de Demencias. Hospital Universitario 12 de Octubre, Madrid. 5-Laboratorio Enfermedades Mitocondriales y Neurometabólicas. Instituto de Investigación Sanitaria Hospital 12 de Octubre, Madrid.
ABSTRACT: The aim of this study is to implement a molecular diagnostic algorithm that allows optimal and cost-effective analysis in ALS and FTD patients in Spain. The number of index cases analyzed was 1156 ALS and 180 FTD, from which a clinical subgroup (ALS-FTD) of 167 patients with both pathologies was split. We propose the primary analysis of C9orf72 for the 5 clinical subgroups, SOD1 for both familial and sporadic ALS, GRN in sporadic FTD, MAPT in familial FTD, and as a major innovation we include TARDBP in the familial ALS and familial FTD groups. In a second line of genetic analysis, we propose TBK1 screening in the ALS-FTD comorbidity group (Gómez-Tortosa et al., 2017; van der Zee et al., 2017) and FUS in early-onset sporadic patients (Bäumer et al., 2010; Chiò, Calvo, et al., 2011; Conte et al., 2012). Finally, in patients with a family history of both ALS and FTD, as well as in cases of ALS-FTD comorbidity, we include the need to perform exome sequencing to find the genetic cause in those patients in whom the primary and secondary analysis was negative or to find cases with more than one causal genetic variant (oligogenesis theory).

7

Inflammasome genes expression as biomarkers in ALS and FTD patients. Expósito-Blázquez, L.1, García-Salamero, G.1, Contreras-Hoyo, I.1, Bellón-Membrilla, S.1, Borrego-Hernández, D.1, Calvo, A.C.2, Herrero-Manso, M.C.2, Cordero-Vázquez, P.1, Villarejo-Galende, A.3, Llamas-Velasco, S.4, González-Sánchez, M.4, Martín-Casanueva, M.A.4, Esteban-Pérez, J.1, Osta, R.2 and García-Redondo, A.1, 1- Neurology department – ALS. Health research Institute, Hospital Universitario 12 de Octubre. Madrid. 2- Aragon 's Institute of Health Sciences (IACS), Faculty of Veterinary, University of Zaragoza. 3- Rheumatology department – Health Research Institute, Hospital 12 de Octubre, Madrid. 4-Neurology department. Health research Institute, Hospital Universitario 12 de Octubre, Madrid. 5-Biochemistry department. Health research Institute, Hospital 12 de Octubre, Madrid.
KEY WORDS: ALS, FTD, biomarkers, inflammation, NLRP3, LGALS1
ABSTRACT: There is a growing need to identify specific biomarkers that facilitate the diagnosis and prognosis of neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Neuroinflammation plays an important role in the pathogenesis of these pathologies (Ching-Hua Lu et al., 2016, Berjaoui, S et al., 2015). The aim of this study is to determine the diagnostic and prognostic capacity of inflammatory genes LGALS1 y NLRP3 as potential biomarkers both on ALS and FTD. Method: This study included a total of 55 ALS patients, 42 FTD patients and 44 healthy controls. Gene expression analysis was performed by quantitative PCR. These levels were related to the main clinical parameters like days since symptoms onset, ALSFRS-r, diagnostic delay, age of onset of symptoms, and others. Statistical analysis was performed using GraphPad Software ®. Results: We found a significant down expression of LGALS1 in FTD patients in respect to the control group. Additionally, NLRP3 expression correlated significantly with diagnostic delay in FTD patients. Conclusions: The expression of LGALS1 was found to be altered in FTD patients, but it could not be considered as a diagnostic biomarker due to the low sensitivity and specificity values shown in the present study. Regarding the functioning of the inflammasome, we have not been able to see an alteration in an important component, NLRP3, on ALS patients. Any case, it would be necessary to

introduce new components related to inflammasome to reach more significant and conclusive results.

8

Long non-coding RNAs as new candidates for diagnostic and prognostic biomarkers in amyotrophic lateral sclerosis (ELA). Tresa López-Royo, Leticia Moreno-García, Laura Moreno-Martínez, Miriam de la Torre, Nora Molina, Paula Aparicio, Mariana Ruiz, Pilar Zaragoza, Ana Cristina Calvo, Janne Markus Toivonen, Alberto García-Redondo, Raquel Manzano, Rosario Osta. LAGENBIO, Departamento de Anatomía, Embriología y Genética Animal, Universidad de Zaragoza, Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Instituto Agroalimentario de of Aragón (IA2), Instituto de Investigación Sanitaria Aragón (IIS), Zaragoza.

ABSTRACT: The lack of sensitive and specific biomarkers for diagnosis and prognosis represents one of the major challenges in Amyotrophic Lateral Sclerosis (ALS), which currently delays its diagnosis and treatment implementation. Genes most frequently mutated in ALS patients (TARDBP, FUS and C9ORF72) have functions related to RNA metabolism, which contributes to neurodegeneration. As key players in this metabolism, long non-coding RNAs (lncRNAs) are regulatory molecules at transcriptional, post-transcriptional and epigenetic levels, yet their knowledge in the context of ALS is very limited. This project aims to unravel the expression profile of lncRNAs in the main tissues affected in ALS, i.e., in the nervous system and muscle, and in serum; and to distinguish it from that of healthy individuals and patients with other neurodegenerative pathologies. All of this in order to find specific diagnostic biomarkers in the disease. The comparison between the results obtained in different tissues and serum will allow extrapolating the results using blood samples, reducing invasiveness at the clinical level. A second objective is to monitor the levels of these lncRNAs at different stages of the disease, as well as to correlate them with individual survival, which would potentially allow the generation of a panel of predictive and disease course biomarkers. For this purpose, this project will use samples obtained from a mouse model of ALS (SOD1-G93A), as well as from patients, which will increase the robustness of the results and their translational potential in clinical practice.

9

Intramuscular inoculation of MTBVAC stimulates T-regulatory cells in the SOD1G93A mouse model. Moreno-Martínez L. (1), Broset E (2), Moreo E (2), Moreno-García L (1), López-Royo T (1), Ruiz M (1), Toivonen JM (1), de la Torre M (1), Molina N (1), Aparicio P (1), Manzano R (1), Zaragoza P (1), Aguiló N (2), Calvo AC (1), Martín C (2), Osta R (1). (1) LAGENBIO, Department of Anatomy, Embryology and Animal Genetics, University of Zaragoza, Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Agroalimentary Institute of Aragon (IA2), Institute of Health Research of Aragon (IIS), Zaragoza. (2) Department of Microbiology, Faculty of Medicine, University of Zaragoza, CIBERES and Research Network on Respiratory Diseases, Zaragoza.

ABSTRACT: Modulation of inflammation in amyotrophic lateral sclerosis (ALS) has been one the main therapeutic approaches studied in the last years. In this line, clinical trials based on stimulating T-regulatory cells (Treg) are currently being developed showing promising results. MTBVAC is a new vaccine against tuberculosis, a live attenuated strain of the human pathogen Mycobacterium tuberculosis, which is able to induce adaptive immune responses. The aim of this study was to assess the effect of MTBVAC on survival rate through the modulation of Treg in the SOD1G93A mouse model. First, we analyzed the

correlation of the number of Treg and survival time of SOD1G93A mice, along with the best route of administration for MTBVAC. Next, we carried out two survival studies with SOD1G93A mice inoculated with MTBVAC at the age of 60 (P60) and 80 (P80) days. Our results showed a positive correlation between the number of Treg in spleen and the survival time of mice. Furthermore, intramuscular inoculation increased the number of Treg in both spleen and lymph nodes more than intraperitoneal inoculation. In both survival studies we could observe that the lifespan of MTBVAC inoculated mice was longer during eighty days post-vaccination. However, that effect disappeared after this period, suggesting that future research could be focused on prolonging the effect of MTBVAC, which could contribute to extending the lifespan of the SOD1G93A mice.

10

Identification of circular RNAs involved in ALS Keywords: circular RNA (circRNA), RNA metabolism, biomarkers, amyotrophic lateral sclerosis (ALS). Leticia Moreno-García, Tresa López-Royo, Laura Moreno-Martínez, Miriam de la Torre, Nora Molina, Paula Aparicio, Mariana Ruiz, Pilar Zaragoza, Alberto García-Redondo, Janne M. Toivonen, Ana Cristina Calvo, Raquel Manzano, Rosario Osta. Department of Anatomy, Embryology and Animal Genetics, University of Zaragoza, Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), Agroalimentary Institute of Aragon (IA2), Institute of Health Research of Aragon (IIS), Zaragoza.

ABSTRACT: There is increasing evidence of the importance of RNA metabolism dysregulation in the etiopathogenesis of ALS. Understanding these events in depth would allow the development of new diagnostic and therapeutic tools, hence we aimed to know the state of expression of circular RNAs (circRNAs) through sequencing studies. Based on the results obtained in the circRNAseq studies, the possible involvement in the disease (circRNAs originated from genes associated with ALS or involved in neurodegenerative processes and CNS development...) and the existing bibliography, we selected the circRNAs with the greatest potential for their study. We detected several significantly altered circRNAs in the spinal cord and skeletal muscle throughout the disease. Among them, two circRNAs negatively correlate with longevity, indicating that the higher their expression, the less animals live. These circRNAs could act as miRNA sponges that regulate the expression of genes related to neuroinflammation described in ALS. Our next objective is to study these circRNAs together with their corresponding miRNAs in blood samples from the murine model and patients in order to also validate their potential as peripheral ALS biomarkers. These results are relevant since they constitute the first study of circRNAseq carried out in an animal model of ALS and from which it has been possible to identify potential circRNAs that could help to understand the etiopathogenesis of the disease, as well as help in clinical practice by facilitating the diagnosis and/or prognosis of patients.

11

ALS_MADRID: A multidisciplinary collaborative project for discovery and development of effective drugs for ALS. Ana Martinez (Project coordinator) Centro de Investigaciones Biológicas-CSIC, Madrid.

KEY WORDS: ALS, TDP-43, kinase inhibitor, celular models, animal models

ABSTRACT: ALS-Madrid is a multidisciplinary and collaborative project supported by the biomedicine program of Madrid Community. ALS-MADRID joins seven different research

groups from different institutions and disciplines, chemistry, biology, pharmacology and clinical experience. We combine basic, translational and clinical experience with the main goal of discovery and development to the clinical setting of new drugs with efficacy shown for ALS therapy. Specifically, we have focused our efforts in small molecules able to recover TDP-43 homeostasis. The nuclear protein TDP-43 has emerged as the main histopathological marker of ALS, both in sporadic and familial origin.

Our more relevant results achieved in the three first year of joint work can be summarized as follows:

1.-Bio-bank formed by immortalized lymphocytes from ALS patients and healthy controls. We have different ALS types both from sporadic origin, and from familiar ones such as SOD1, c90rf72, TBK1 and TARDBP. These human-based cell cultures recapitulate TDP-43 pathology offering a useful platform not only for drug Discovery but also for search a personalized treatment for ALS patients

2.-Protein kinase inhibitors development, mainly CK1 and CDC7 inhibitors, showing efficacy as modulators of TDP-43 pathology in cellular and animal models. One of these candidates has been transferred to a biotech company for regulatory development to clinical trials.

3.-Tideglusib, a GSK3 inhibitor, repurposing for ALS therapy. The clinical trial phase II for ALS is in the last steps for approval in Switzerland.

In the last year of our joint research program we hope to finally show the therapeutic relevance of these new TDP-43 modulators not only for ALS but also for FTD, as both rare diseases are a continuum of the same pathology.

SOCIAL COMMUNICATIONS

1

Protocol of action of neurological social work with patients with als and their families, from diagnosis to grievance. Dra. Doña Mª José Aguilar Idáñez (1), Doña Verónica Olmedo Vega (2). (1) Universidad de Castilla-La Mancha; (2) Hospital Clínico Universitario de Valladolid.

KEYWORDS: Neurological Social Work, ELA, Family, Quality of Life and Systematized Professional Intervention.

ABSTRACT: People with ALS and their families require socio-sanitary intervention during the period of time that ranges from the moment of diagnosis to the end of the family grief, caused by the death of the patient.

Neurological Social Work, as a professional member of the multidisciplinary team of ALS patient care at the Hospital, is a key figure in providing an adequate response to numerous specific problems and situations that ALS patients and their families present. Circumstances that require specialized and personalized interventions, which must be carried out in a coordinated, sequenced and coherent manner through a protocol that guides professional intervention. A professional intervention systematized and adapted to the scope and evolution of the condition in each specific case and that responds to their needs, considering the wishes and will of the affected people. The intervention of the

neurological social worker will always be necessarily based on the specific knowledge of the disease suffered by the intervened person and the scientific evidence in this regard.

A specific protocol of action of Neurological Social Work developed at the Hospital Clínico Universitario de Valladolid is presented, implemented from the diagnosis of the disease to the family mourning caused by the loss, which incorporates as a central axis the active participation of the patient and his family in the intervention process, as main protagonists of their own life.

The specific knowledge of the disease by the Neurological Social Work professional, together with the design and implementation of the action protocol, allows the specific needs of each patient and their families to be assessed with socially effective criteria, providing them with the necessary support in the precise moment, something essential to contribute to your quality of life.

2

Sheltered Accommodation Affected by ELA. Barbara Chiralt. Adela Comunidad Valenciana.

KEYWORDS: Sheltered Accommodation, quality of life, self-management, ALS, specialization, coexistence.

ABSTRACT: The project "creation of a sheltered home for those affected by ALS" responds to the need to create specialized resources for people with ALS with which to provide care that guarantees their quality of life and to face a health and social gap. The novelty and suitability of the resource is given by the intensity of dedication to those affected and by specialization (large dependents with dysphagia problems and respiratory failure), with the additional benefit of being a more standardized resource than residential care, and of reduced dimensions that facilitate self-management by the beneficiaries themselves. The beneficiaries will be mixed: from 4 to 7 people with ALS of different age ranges, large dependents, without the necessary resources to guarantee adequate care to their degree of affectation. A need is estimated between 2% and 5% of those affected in the Valencian Community. A distribution of four assistants in the morning, three in the afternoon and two at night, has been estimated to serve 7 beneficiaries. Obtaining the space is established through its assignment, remodelling and equipment by the Public Administration and through private financing. The economic viability of the project depends on its incorporation into the social concert. The spaces would contemplate the distribution in individual rooms with home automation systems that facilitate a certain degree of autonomy and intimacy to the beneficiaries and common spaces where they can interact and coexist.