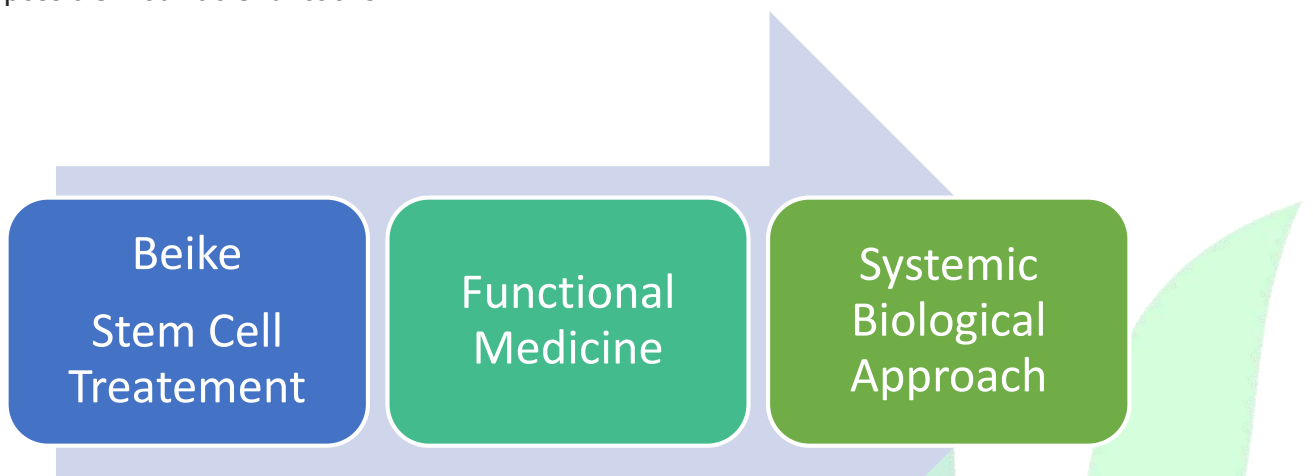


## ALS SYSTEMIC BIOLOGY APPROACH

Beike is providing a unique combination of **stem cell treatment**, extensive rehabilitation through **Functional Medicine**, and a **Systemic Biological Approach** for ALS patients in our partner hospital in Bangkok, Better Being Hospital.

By using the systemic biological approach we view the condition as the continuum of genetic/ environmental/ lifestyle interactions, resulting in ongoing physiological imbalances and eventually leading to collective clinical presentations. Management by this approach is extending upstream to the pathophysiology and pathogenesis stage and tries to work with all possible modifiable functions.



Laboratory testing, patient history, family history and extensive medical investigations are conducted which include:

### **Genetic Predisposition workup (Selected from below)**

- Detoxigenomic Profile® screening for Single Nucleotide Polymorphisms(SNPs) of particular genes ,including SOD1,SOD2,MTHFR,COMT,NAT,GSTM,GSTP , CYP1A1 CYP2A6 CYP2E1 CYP1C19,CYP1B1 CYP2D6 CYP2C9 CYP3A4
- Immunogenomic Profile® screening for Single Nucleotide Polymorphisms(SNPs) of particular genes , including IL-1 $\beta$  ,TNF-alpha, IL-4,IL-6 ,IL-10 ,IL-13

### **Other possible SNPs panels (Selected from the list below)**

- Environmental/ Life Style factors
- Drinking Water Analysis
- Whole blood toxic element analysis
- Core toxic Panel

## Ongoing Physiological Imbalances (Selected from the list below)

### Oxidative Damage Markers

- Mitochondria function assessment by Organic Acid Analysis
- Negalase test, Ann Connelly test
- Neopterin/Biopterin Profile
- Blood inflammatory markers
- Work up for possible autoimmunity, such as Immuglobulin E,G,A,M analysis and Food Antibody Profile
- Work up for possible toxic accumulation , such as Red Cell toxic element profile
- Liver caffeine/aspirin/acetaminophen challenge test
- Comprehensive hormonal profile
- Neurotransmitter Profile
- Methylation/Sulfation Analysis
- Comprehensive Digestive Analysis
- Amino Acid Profile
- Fatty Acid Profile

### Clinical symptoms management (Selected from the list below)

- Muscle enzymes (serum creatine kinase, ALT, AST, LDH)
- Serum creatinine
- Electrolyte , particularly looking for Hypochloremia, increased bicarbonate, CSF protein

## Management:

After collecting all relevant information, personalized management plan will then be designed aiming at working with possible modifiable factors, ranging from dietary modification, specific environmental control, nutritional management, supplementation, immunologic modulation, physical rehabilitation, occupational therapy to variety of possible regenerative procedures. The management plan will be aimed at controlling of present illness progression by modulation the ongoing pathophysiologic processes, manage all modifiable pathogenesis factors and find options to help reversing the damaged from illness processes. This management should be done together with standard care and should provide more beneficial overall outcome to the patient.

## Stem Cell Treatment:

Human umbilical cord blood (UCB) cells have been shown to have neuroprotective and therapeutic benefit in SOD1 mice (ALS model) possibly through the active involvement of these cells in inhibiting the host immune/inflammatory response (i.e. cytokines). UCB stem cells act through immunomodulation and neuroprotection by modulation of the autoimmune process.

Mesenchymal stem cells (MSCs) are very attractive multipotent stem cells for ALS cell therapy because of their great plasticity and their ability to provide the host tissue with growth factors or to modulate the host immune system. MSC transplantation increases neuron survival and prevents astrogliosis and microglia activation as Astrocytes are both the target and cause of neuroinflammation, MSCs can rescue neurons and oligodendrocytes from apoptosis through the release of trophic and anti-apoptotic molecules, resulting in the induction of a neuroprotective microenvironment. In addition, MSCs can promote the proliferation and maturation of local neural precursor cells, leading to their differentiation into mature neurons and oligodendrocytes.



## Diet and Nutritional Management:

Study showed that nutritional factors that associated with reduced survival were weight loss, malnutrition and severe dysphagia. Vitamin E, folic acid, alpha lipoic acid, lyophilized red wine, coenzyme Q10, epigallocatechin gallate, Ginkgo biloba, melatonin, Cu chelators, and regular low and moderate intensity exercise, as well as treatments with catalase and l-carnitine, hold promise to mitigating the effects of ALS.

Currently available evidence supports the potential role of dietary interventions as a therapeutic tool for amyotrophic lateral sclerosis. Ketogenic Diet (KD) Plan showed to alter the progression of the clinical and biological manifestations of the G93A SOD1 transgenic mouse model of ALS. These effects may be due to the ability of ketone bodies to promote ATP synthesis and bypass inhibition of complex I in the mitochondrial respiratory chain.

## Physical Activities:

In the earlier stages of ALS, many people have found both physiological and psychological boosts from various types of physical exercise for disused muscles. Proper

Exercise is important for preventing atrophy of muscles from disuse, which is the key for remaining mobile for as long as possible, and as long as it is possible to exercise comfortably and safely, for preserving cardiovascular fitness.

However, the typical neuromuscular patient features a great physical inactivity and disuse weakness, and for that reason many controversial authors have contested exercise in these patients during years, especially in ALS which is rapidly progressive. There is ongoing controversy on the real risks or benefits of this.

Evidence suggests that moderate exercise is not associated with adverse outcomes in persons with early-stage ALS. Moderate exercise programs can be safely adapted to abilities, interests, specific response to exercise, accessibility, and family support.(8) Recent research studies document significant benefits in terms of survival and quality of life in ALS.

Sedentary barriers such as early fatigue and inherent muscle misuse should be overcome, for instance with body-weight supporting systems or non-invasive ventilation, and exercise should be faced as a potential non-monotonous way for contributing to better health-related quality of life. Variety of physical and occupational therapy intervention are beneficial to persons with ALS.

For diet and physical activities in summary, caloric restriction, malnutrition and high-intensity exercise are contraindicated in ALS.



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