Letter to the Editor

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Laboratory biomarkers and frailty: presentation of the FRAILOMIC initiative

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To the Editor,

Frailty is traditionally defined as a specific geriatric syndrome characterised by increased vulnerability to unfavourable outcomes, such as falls, disability, hospitalisation and overall mortality, which is a result of the impairment of manifold and interrelating biological pathways, ultimately leading to decreased homoeostatic reserve and lower resistance to stressor events, such as therapy or infections [1]. Due to an increasing trend toward ageing of the population (the percentage of people aged ≥65 years is projected to increase by 20% in Europe by 2060), frailty will soon emerge as a serious and increasingly important global health burden [2].

Several lines of evidence attest that frailty can be prevented, or at least delayed, by the establishment of timely and appropriate physical, psychological and therapeutic interventions [3]. The two main drawbacks in managing frailty are the still uncertain definition of this condition, and the challenging clinical assessment (i.e., loss of muscle mass and strength, decay of energy and exercise tolerance, decreased physiological reserve), which makes it impractical for routine use in clinical practice [4]. As for other chronic and prevalent disorders [5, 6], laboratory diagnostics have the potential to help identify those individuals who may be at greater risk of developing this condition later in life, and may also assist the managed care of frail individuals [7]. Over the last few decades many independent studies have attempted to identify predictive, diagnostic and prognostic biomarkers of frailty (i.e., vitamin D, cortisol, testosterone, dehydroepiandrosterone and inflammatory biomarkers among others), but no definitive conclusions can be drawn. This is principally attributable to limitations of the published trials, such as the small sample size, the heterogeneity of entry points and study population, and the use of little validated techniques for biomarker measurement [8].

The FRAILOMIC consortium (available at: http://www.frailomic.org/) was created and funded under the European FP7 framework in order to overcome these limitations. The consortium comprises seven small and medium-sized companies, six universities, two leading research centres, two hospital-based research groups and researches affiliated with the World Health Organization (WHO). The primary aim is to create a European network for developing clinical tools and validating biomarkers that can assist in the managed care of frailty. More specifically, a large number of molecular and biochemical biomarkers will be measured in as many as 75,000 participants (Table 1), in order to develop predictive, diagnostic and prognostic

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Table 1: Molecular and biochemical biomarkers that will be tested in the FRAILOMIC initiative.

Biological pathway	Biomarker/target
Muscle function/energy metabolism/inflammation	Ciliary neurotrophic factor
	Mitochondrial DNA
	Angiotensin converting enzyme insertion/deletion
	α-Actinin 3
	Angiotensinogen
	Vitamin D receptor
	Estradiol
	Growth differentiation factor 8 (myostatin)
	Activin-A
	C-reactive protein (CRP)
	Interleukin-6 (IL-6)
	Tumour necrosis factor-α (TNF-α)
	Soluble urokinase-type plasminogen activator receptor (SUPAR)
	Procalcitonin (PCT)
	sE Selectin
	Soluble vascular cell adhesion molecule (sVCAM1)
	Intercellular adhesion molecule-1 (ICAM)
	Vascular endothelial growth factor (VEGF)
	Matrix metallopeptidase 9 (MMP-9)
	Matrix metallopeptidase 11 (MMP-11)
	Myeloperoxidase (MPO)
	Antinuclear antibodies
Vascular ageing	Nitric oxide synthase
	Superoxide dismutase
	Galectin-3
	Prohormone brain natriuretic peptide (proBNP)
	High-sensitivity troponin T
	Oxidised low density lipoproteins (Ox-LDL)
	Adiponectin
Osteoporosis	Vitamin D
	C-terminal telopeptides of type II
	Collagen
	Procollagen II C-Propeptide
SIRT/p53 pathway	Peroxisome
	Tumour protein 53
	Sestrin 2
	Sirtuin
Insulin signalling pathway	RAC-α serine/threonine-protein kinase, mTOR, FOXO
	Mammalian target of rapamycin
	Forkhead box O
Longevity-associated microRNA (miRNAs)	miR-24, miR-130, miR-94
Ageing and senescence-associated miRNAs	miR-17, miR-19b, miR-20a, and miR-106a
Osteoporosis-related circulating miRNAs	mir-31miR-10a-5p, miR-10b-5p, miR-22-3p, miR-133b, miR-328-3p, let-7g-5p

models in the older general population and people at a higher risk of frailty. The analytical and diagnostic performance of these biomarkers will be compared against the current quality specifications to define whether the current techniques are suitable for use in this specific population [9, 10]. A selected set of biomarkers will then be validated prospectively and assessed to identify the best fit models, which will guide the development of panels of tests or risk estimation models to be used in the clinical setting. The homeostatic impairments of frailty will hence be assessed using a multidisciplinary approach within this network. Hopefully, the outcomes of this initiative will underline the important contribution of laboratory diagnostics for reducing the prevalence or severity of this increasingly frequent condition, thus resulting in large benefits for individuals, society and healthcare systems.

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