

## Supplementary file 1

**Table S1. Enzymes and transporters in creatinine biosynthesis**

<b>Protein (Abbreviated name)</b>	<b>L-arginine-glycine amidinotransferase (AGAT)</b>	<b>Guanidoacetate methyltransferase (GAMT)</b>	<b>Creatine transporter/ <i>SLC6A8</i></b>	<b>Creatine kinase (CK)</b>
<b>Tissue Distribution</b>	Kidneys, Pancreas, Liver (cow, pig, monkey, and human), heart, lung, spleen, muscle, brain, testis, and thymus	Liver, Pancreas, Testis, Caput epididymis, Ovary, spleen, heart, skeletal muscle, lung, kidney	Skeletal muscle, Kidney, Heart, brain	Skeletal muscle, Myocardium, Smooth muscle, Brain, Gastrointestinal tract, Lung, Kidney.
<b>Substrate</b>	L-arginine, glycine	Guanidoacetate	Creatine (but not creatinine)	Creatine
<b>Inhibitor</b>	L-Ornithine, Creatine, Cyclocreatine, N-acetimidoysarcosine, N-ethylguanidinoacetate, Estrogens Diethylstilbestrol, Methyltestosterone	/	Creatine, Guanidinoacetate, Guanidinopropionate, 3-guanidinobutyrate, Estrogen, Cycloheximide, Cyclocreatine, Ouabain, Digoxin	Nitric oxide, AMP-activated protein kinase
<b>Inducer</b>	Testosterone, Thyroxine, Growth hormone, Testosterone, Estrogen	/	Isoproterenol, Norepinephrine, N6,2'-O-dibutyryl adenosine 3',5'-cyclic monophosphate, Insulin, Insulin-like growth factor I, 3,3',5'-triiodothyronine, Amylin, Testosterone	$\beta$ -guanidino propionic acid,
<b>Diet or disease</b>	Fasting $\downarrow$ , protein-free diets $\downarrow$ , Vitamin E deficiency $\downarrow$ , Streptozotocin-induced diabetes $\downarrow$ , Thyroidectomy $\downarrow$ , Hypophysectomy $\downarrow$ , Chronic renal	Hepatocarcinoma $\downarrow$ , Alloxan induced-diabetic $\downarrow$	Diet containing creatine $\downarrow$ , 3,3',5'-triiodothyronine-induced creatinuria $\downarrow$ , Cell energy depletion $\downarrow$	Muscle damage and necrosis $\uparrow$ , Facioscapulohumeral dystrophy $\uparrow$ , Muscular dystrophy $\uparrow$ , Hypothyroidism $\uparrow$ , Infective

	failure ↓			rhabdomyolysis↑, Oxidative and radical damage ↑, Alzheimer's disease↓, Pick's disease↓
<b>References</b>	(Hoberman et al., 1948; Van Pilsum and Wahman, 1960; Fitch et al., 1961; Walker, 1979; Funahashi et al., 1981; Van Pilsum et al., 1982; Levillain et al., 1995; Wyss and Kaddurah-Daouk, 2000)	(Van Pilsum et al., 1972; Walker, 1979; Yanokura and Tsukada, 1982; Henderson et al., 1983; Wyss and Kaddurah-Daouk, 2000; Joncquel-Chevalier Curt et al., 2015)	(Gonda and Quastel, 1962; Kurahashi and Kuroshima, 1977; Loike et al., 1988; Bennett et al., 1994; Odoom et al., 1996; Guerrero-Ontiveros and Wallimann, 1998; Steenge et al., 1998; Wyss and Kaddurah-Daouk, 2000; Joncquel-Chevalier Curt et al., 2015)	(Aksenov et al., 1997; Ponticos et al., 1998; Kaasik et al., 1999; Brancaccio et al., 2007)

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