Table S1 Summary of molecular effects induced by T/DHT supraphysiological doses in *in vitro* and *in vivo* systems

System	Supraphysiological treatment	Biological effect	Molecular targets	Reference
Neonatal rat ventricular cardiomyocytes	10 µM	T-type Ca^{2+} current	$Ca_v3.1$, $Ca_v3.2$	91
Neonatal and adult rat ventricular cardiomyocytes	100 nM	L-type Ca^{2+} current	$Ca_v1.2$	92
Rat aortic smooth muscle cell line (A7r5)	275 µM	L- and T-type Ca^{2+} current	$Ca_v1.2$, $Ca_v3.2$	93
Adult rat ventricular cardiomyocytes	100 nM	L-type Ca^{2+} current	$Ca_v1.2$	94
Neonatal rat ventricular cardiomyocytes	10 µM	Cardioprotection	Flavoproteins, mitoK_{ATP}	97
Human radial artery	Up to 300 µM	Vasorelaxation	K_{ATP}	98
Rat aorta	1 nM - 1 mM	Vasorelaxation, inhibits Ca^{2+} influx.	K_{Ca}	99
HAECs	Up to 3,5 µM	Vasodilatation	ADM	100
HAECs	Up to 3,5 µM	Vasoconstriction	Endothelin-1	101
Rhesus monkeys	50 mg/inj/2wks; 32 months	Liver function parameters	HDL, LDL, SGOT, SGPT	106
Healthy human adults	600 mg/inj/wk; 16 wks	Not determined	HDL, ApoA1	107
Eugonadal, obese, elderly men	600 mg/wk; 3 wks	Not determined	HL, HDL, LDL, SHBG	108
HEPG2 HMDMs	100 ng/ml	Choletserol transport	SR-B1 HL	114
HMDMs	10 nM / 100 nM	Reduced expression of cytokines	TNF-α; IL-1b	116
HUVECs	1 µM	Opposing effects based on the inflammatory status	UCN1, p38/MAPK, ERK1/2, NF-kB	117

HUVECs	Up to 1 µM	Inflammation	VCAM-1	119
HAECs	100 nM, 1 µM	Vasodilation	VCAM-1	120
HUVECs	Up to 100 nM	Proapoptotic factor	Bcl-2	121
HUVECs	0,1 - 9,6 µM	Proapoptotic factor	JNK; p38/MAPK	123
Granulose cells	Up to 300 nM	Proapoptotic factor	Cyclin D2; AMPK	124,125
HK-2; PTECs	Up to 1 mM	Proapoptotic factor	Fas; FADD, FasL	126
SH-SY5Y	100 nM/1 µM / 10 µM	Proapoptotic factor	$InsP_3R$	130,133
Seminiferi tubules	100 nM/1 µM	Antiapoptotic factor	CHECK	134
CGCs	500 µg/0,05 ml inj	Antiapoptotic factor	SOD; Catalase	135,136
PBLs	0,7 µg/ml	Antiapoptotic factor	Bcl-2; Caspase-3; STAT5A; Gsn; et al	140
PBLs	0,7 µg/ml	Antiapoptotic factor	Bcl-2; Caspase-3; FAK; Cytokines; paxillin signaling	141
Healthy human adults	600 mg/inj/wk; 20wks	Not determined	IGF-1, Hb	142
PBLs	0,7 µg/ml	Up-regulation of gene involved in skeletal muscle disorders and in cell-mediated immunological response	IDO1; CXCL13; CCL1; GZMB; VDR; ILR2A	143

Table S2 Summary of molecular effects induced by GH/IGF-1 supraphysiological doses in *in vitro* and *in vivo* systems

System	Supraphysiological treatment	Molecular and biological effect	Molecular target	Reference
Bovine blastocysts	1000 ng/ml IGF-1 stimulation for 24 h	Increased apoptosis and number of cells in the inner cell mass (ICM)	TP53, IGF-1R	145
Mouse fibroblasts	50 nM IGF-1 stimulation for 3-24 h	Anti-apoptotic effects	TDAG51	149
Human PBLs	1.25 µg/ml IGF-1 hyperstimulation	Active cytoskeletal reorganization and transendothelial migration	STAT-1, cytokines	150
Human PBLs	1.25 µg/ml IGF-1 hyperstimulation	Up-regulation of gene involved in skeletal muscle disorders and in cell-mediated immunological response	FNI, RAB31	143
Recreational athletes (males and females)	GH supraphysiological doses for 8 weeks (1 mg/day I week-1.5 mg/die II week and 2 mg/die for 6 week)	Modest transcriptional effects of GH-treatment similar in magnitudo to the variation between individuals.	HSPC159, ITGB3, OLFM4	154
Liver transgenic mice over-expressing bovine GH	Liver GH overexpression after microinjection of PEPCK-GH plasmid into the germ line	Alterations in the liver signaling pathways involved in cell growth, proliferation and survival that resemble those found in many human tumors.	Akt2, NFκB, GSK3β, β-catenin, cyclin D1, cyclin E, c-myc, c-jun and c-fos	158,159
Healthy adult male rats	Long-term (24 weeks) GH gene therapy after injection of adenoviral CMV-GH1 vector	Modification of genes associated with angiogenesis, oncogenesis, apoptosis, immune networks, signaling pathways, metabolism, cell adhesion molecules, and cytokine-cytokine receptor interaction.	Pla2g2a, Rap1B, Nfkbia	160
Mouse	IGF-1	Marked muscle	Structural proteins	161

model	overexpression mediated by AAV vectors gene transfer	hypertrophy, neovascularization and fast-to-slow fiber type transition	Energy metabolism enzymes	
Healthy human adults	GH supraphysiological doses-1 month (0.067 mg/kg/day)	Not determined	IGFBP-4 IGFBP-5	162