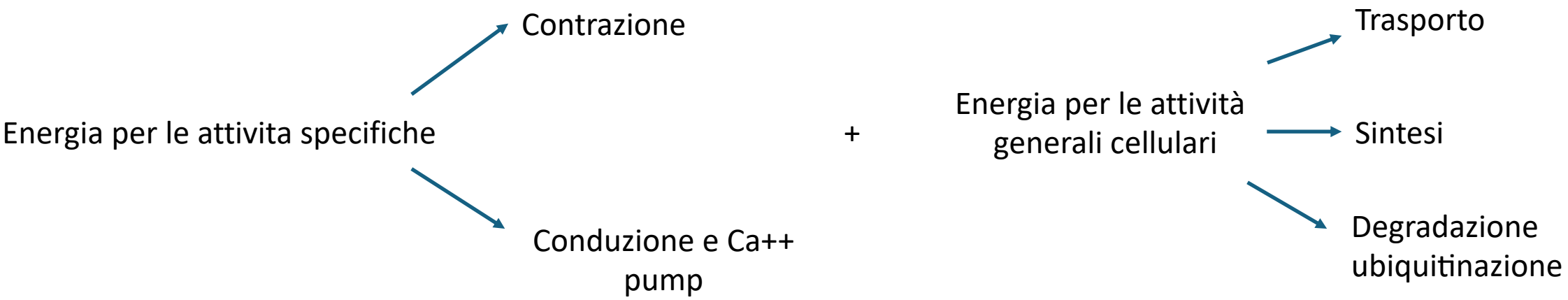
IL TRAPIANTO CARDIACO: LA FASE CRITICA DEL PASSAGGIO DAL DONATORE AL RICEVENTE

13.00	Cenni sul metabolismo del cuore: un organo onnivoro - ***Vittorio Bellotti***
13.15	Il trapianto: sistemi di conservazione, trasporto e protezione del cuore dal prelievo al donatore all'arrivo in sala operatoria per l'impianto al ricevente - ***Carlo Pellegrini***
13.30	Il trapianto: la preparazione del ricevente, l'impianto e le prime risposte sulla funzionalità e performance - ***Stefano Pelenghi***
13.45	Il decorso in Terapia Intensiva Cardiotoracica del paziente appena sottoposto a trapianto di cuore: luci e ombre sul futuro del nuovo organo - ***Mirko Belliato***

The heart is a metabolic **omnivore** and the adult heart selects the substrate best suited for each circumstance, with fatty acid oxidation preferred in order to fulfil the high energy demand of the contracting myocardium. The fetal heart exists in an hypoxic environment and obtains the bulk of its energy via glycolysis.

20-30% of myocyte volume is occupied by mitochondria



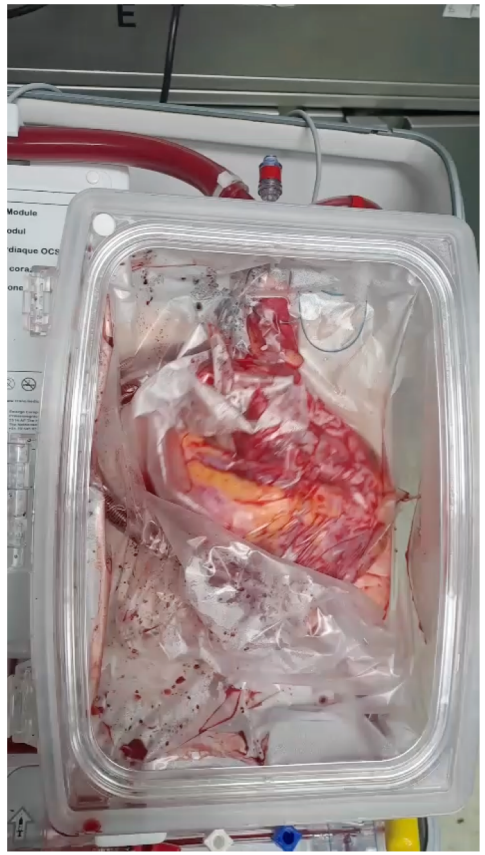
IL TRAPIANTO CARDIACO: **LA FASE CRITICA DEL PASSAGGIO DAL DONATORE AL RICEVENTE**

Due scenari metabolici diversi

Fermare il metabolismo e
La contrazione
4° C sterile e senza
contatto diretto con il
ghiaccio.

CELSIOR SOLUTION

- Glutatione 3 mM
- Mannitolo 60 mM
- Acido lattobionico 80 mM
- Acido Glutammico 20mM
- Sodio Idrossido 100 mM
- CaCl2 0,25 mM
- KCl 15 mM
- MgCl 13 mM
- Istidina 30mM
- pH 7.3



Metabolismo attivo
Organ Care System Heart
(OCS). 37 °C.

Sangue intero (donatore)
Ematocrito tipicamente ridotto (~20–25%)
Hb 5-7 g/dl
Glucosio 90-180 mg/dl
Insulina 10-50 U/L
Lattato 1-3 mmol/L
FA (non aggiunti)
PO2 > 100 mmHg
Saturazione Hb 95%
pH 7.35-7.45

Cenni sul metabolismo del cuore: un organo onnivoro

Il CUORE TRAPIANTABILE

- Assenza di patologie trasmissibili (neoplasie, HIV, infezioni da germi multiresistenti)
- Compatibilità AB0
- Assenza di antigeni HLA verso cui il ricevente è immunizzato (cross-match virtuale e/o cross-match citotossico)
- Donatori a cuore battente (DBD): morte accertata con criterio neurologico. Sino al maggio 2023 unica tipologia di donatori
- Donatori a cuore non battente (DCD): morte accertata con criterio cardiaco per donatori controllati (tipo 2 di Maastricht). Sino ad ora utilizzati in 4 casi a Pavia (in totale in Italia utilizzati dal maggio 2023 82 donatori)

Sul donatore

- Elettrocardiogramma
- Ecocardiogramma
  - adeguata funzione cardiaca (FE > 50 %)
  - assenza di significativi difetti valvolari o strutturali
- Coronarografia (uomini: > 40 anni, donne: > 45 anni)
- Determinazione della troponina sierica
- Supporto farmacologico inotropo o vasoattivo ridotto (no adrenalina e noradrenalina < 0.2 mcg/kg/min

In OCS

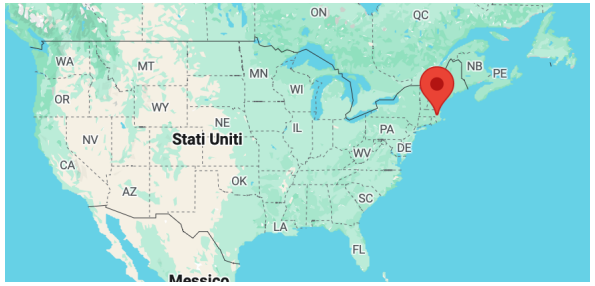
- Frequenza cardiaca (HR)
- Pressione aortica
- Flusso coronarico
- Contrattilità (visiva)
- Lattato arterioso e venoso
- Produzione di CO_2
- pH
- Elettroliti (K^+, Na^+, Ca^{2+})
- Glucosio (incrementabile)

La sfida OCS

Descrizione Azienda

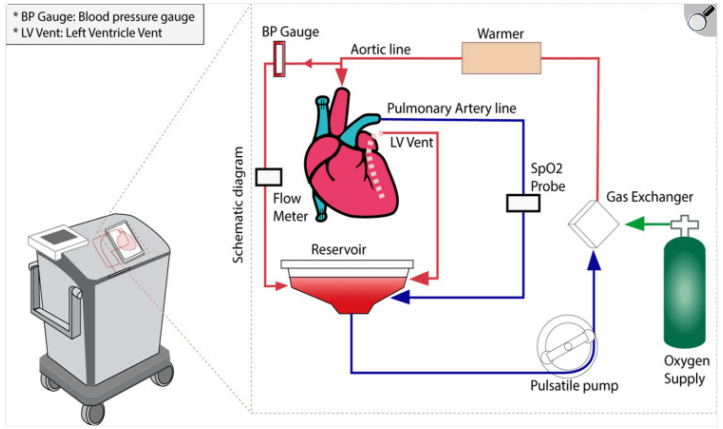
TransMedics

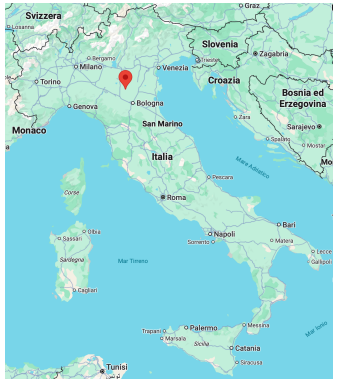
Via Augusto Righi 28
41037 Mirandola (Mo)
E-mail: rbocchi@transmedics.com
Website:https://www.transmedics.com/



1 giorno	1 settimana	1 mese	3 mesi	6 mesi	1 anno	5 anni	Max.
+2,05%	+5,78%	-6,32%	-19,49%	+2,73%	+32,69%	+319,28%	+471,26%

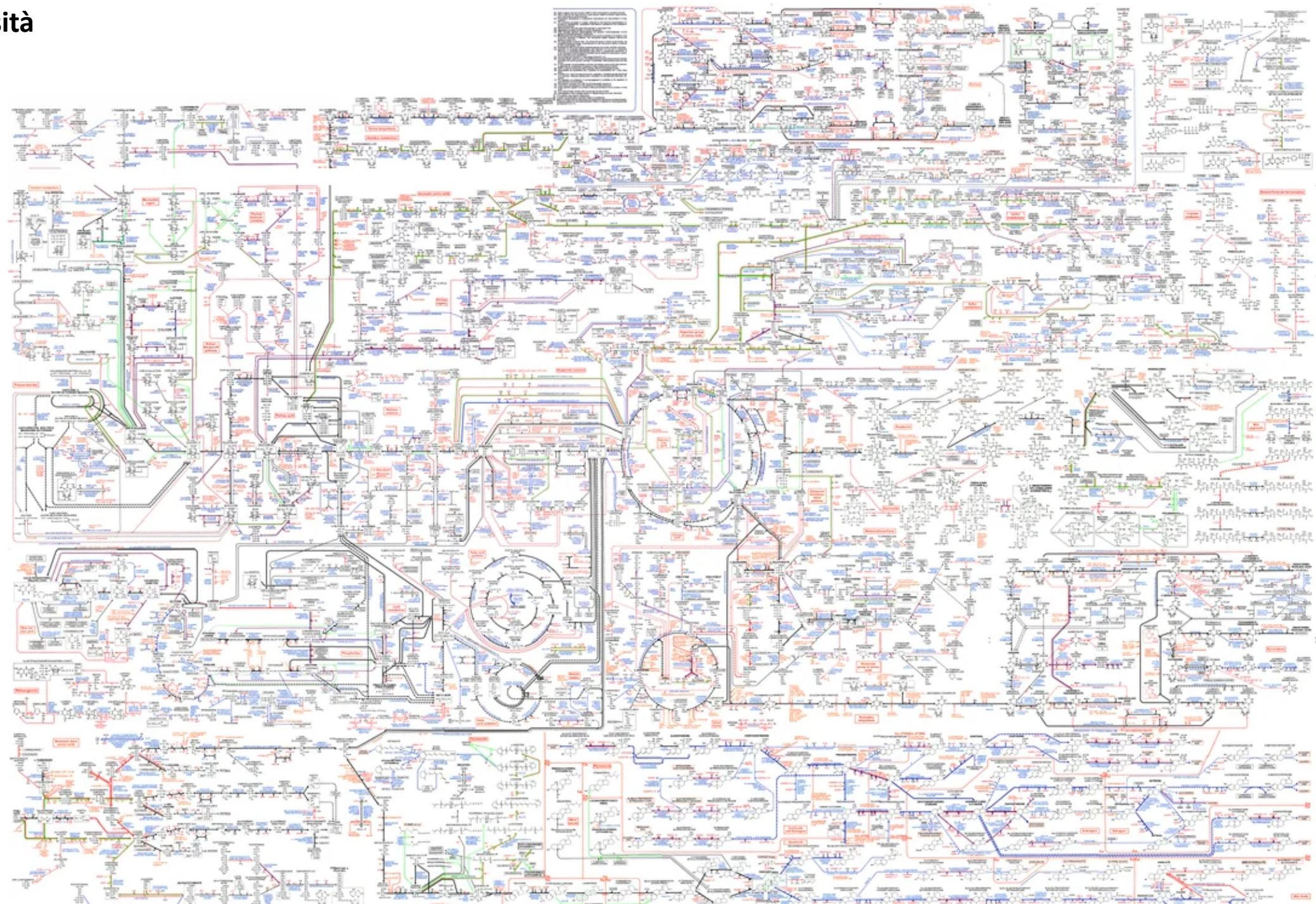
Figure 1. This Figure illustrates an Organ Care System (OCS) heart machine on the left with the schematic diagram on the right, breaking down the processes involved.



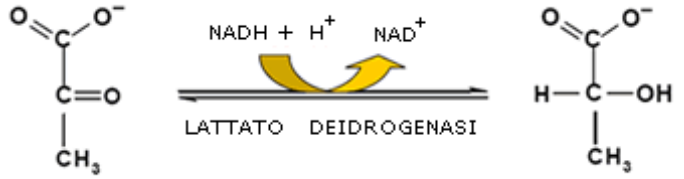


The aorta is connected to the aortic line, the pulmonary artery is connected to the pulmonary artery line (PA line), the left atrium is opened, and the left ventricle is vented via a left ventricle vent (LV vent). The superior and inferior vena cava are ligated. Blood from the PA line and LV vent goes to the reservoir and is pumped to the gas exchanger where it is oxygenated, passed through a warmer, and returned to the heart through the aortic line. The blood pressure, SpO2 (oxygen saturation), and flow rate are all measured during the blood circulation through the different lines. This ensures that the heart receives continuous blood circulation, and all the parameters of the heart are continuously monitored and maintained within narrow margins.

Complessità
2 esempi

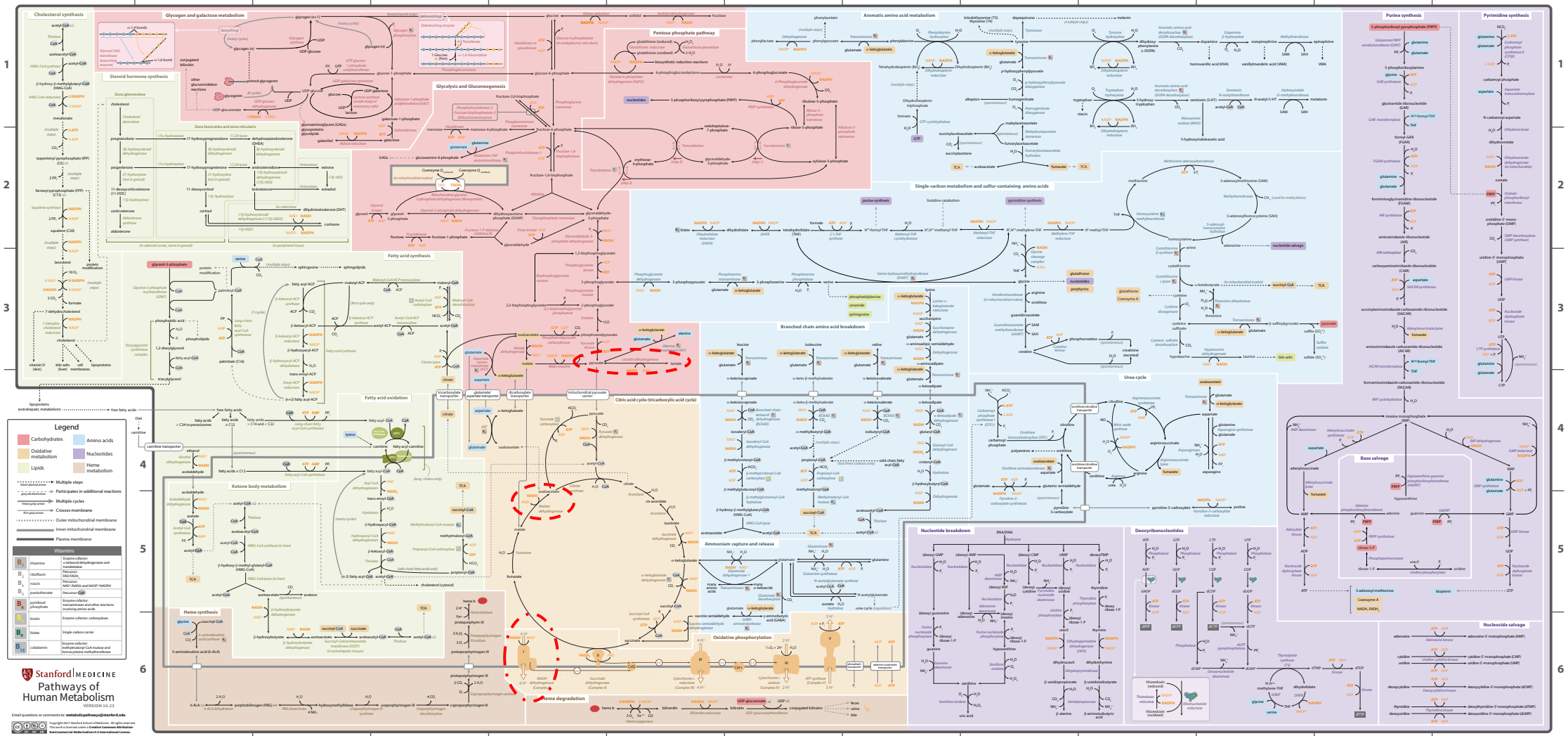


Il lattato



Piruvato
(cheto-acido)

Lattato
(ossi-acido)



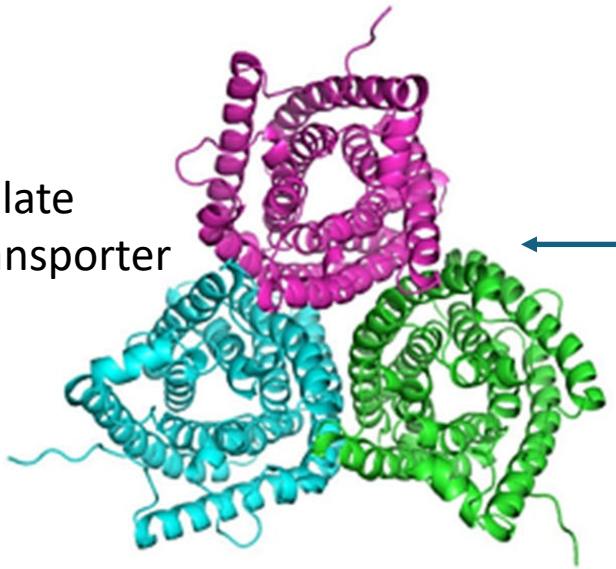
Lattato + **NAD⁺** ⇌ **Piruvato + NADH**

Non può entrare nel mitocondrio

Entra nel mitocondrio

Citoplasma

Malato deidrogenasi



Malate transporter

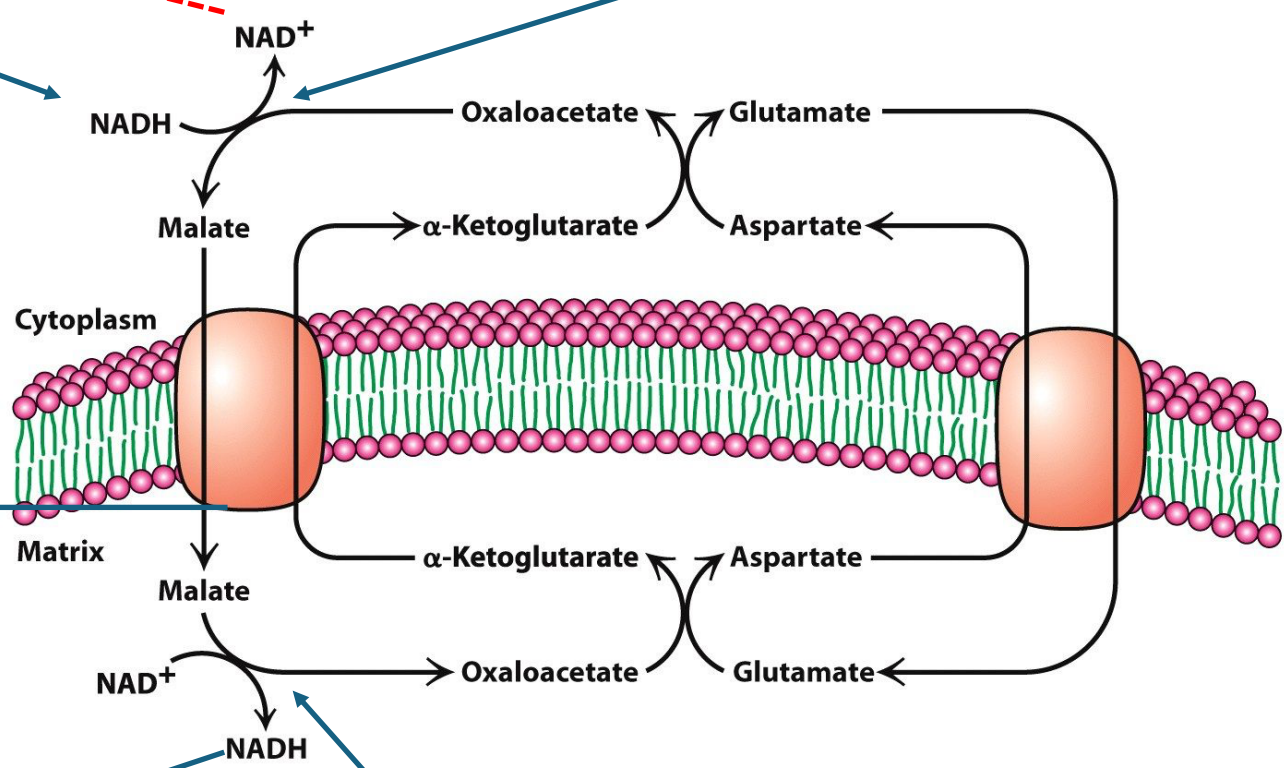


Figure 19.35
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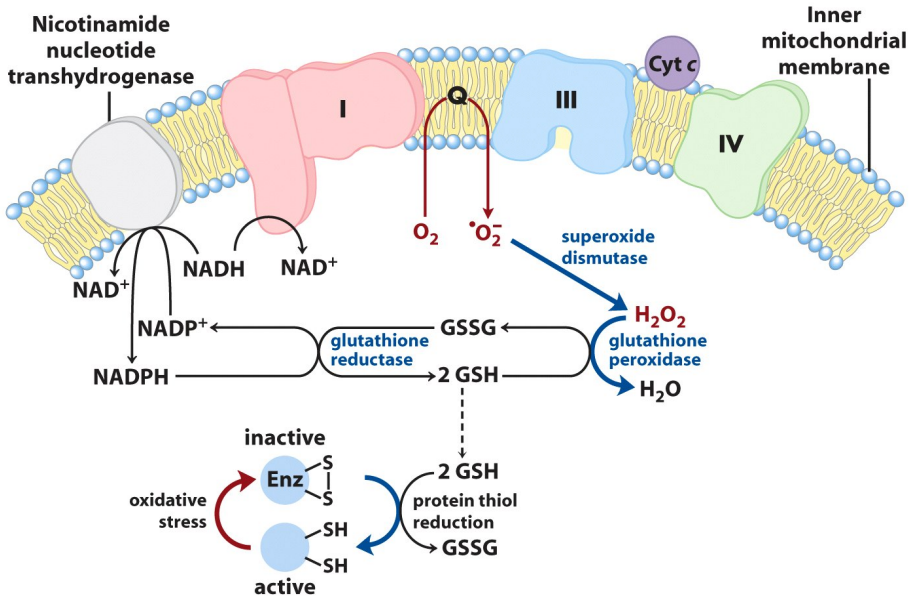
Mitocondrio

I complesso fosforilazione ossidativa

Malato deidrogenasi

Lo stress ossidativo

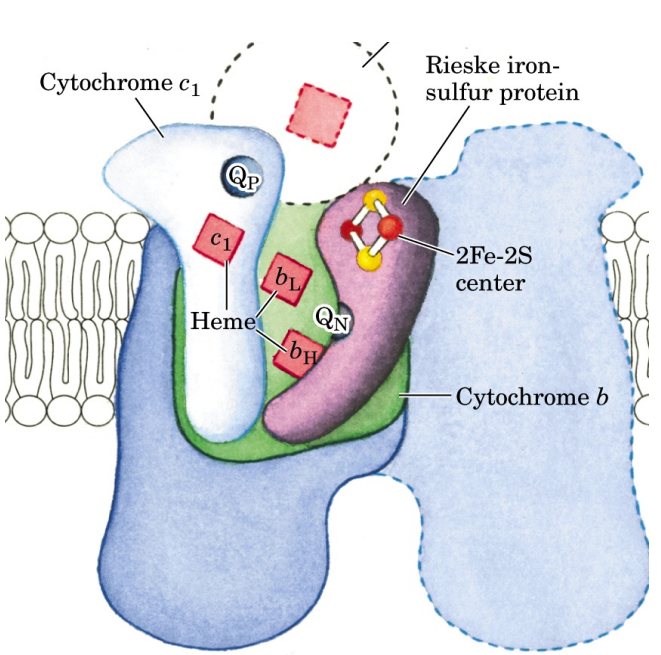


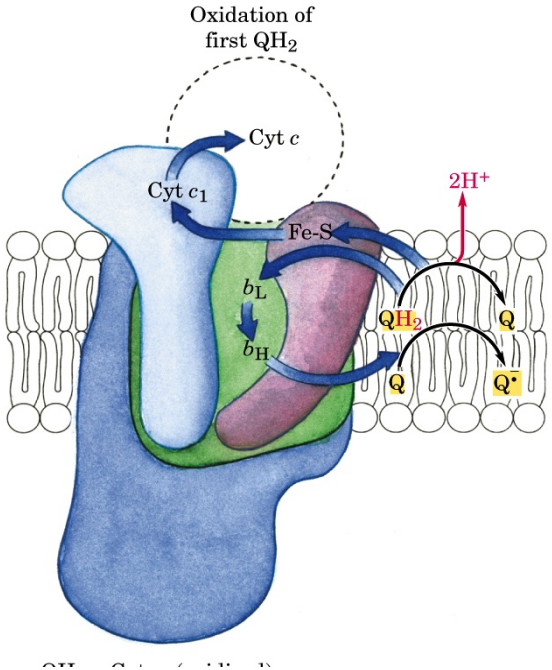
superoxide ion (O2(•-), hydroxyl radical (OH(•)) and nitric oxide (NO(•)

non-radicals hydrogen peroxide (H2O2)

O2•− can be converted to hydrogen peroxide (H2O2) through spontaneous dismutation or enzymatically via superoxide dismutase (SOD)

The main sites of ROS formation in mitochondria are FMN of complex I and semiquinone bound to the QN site





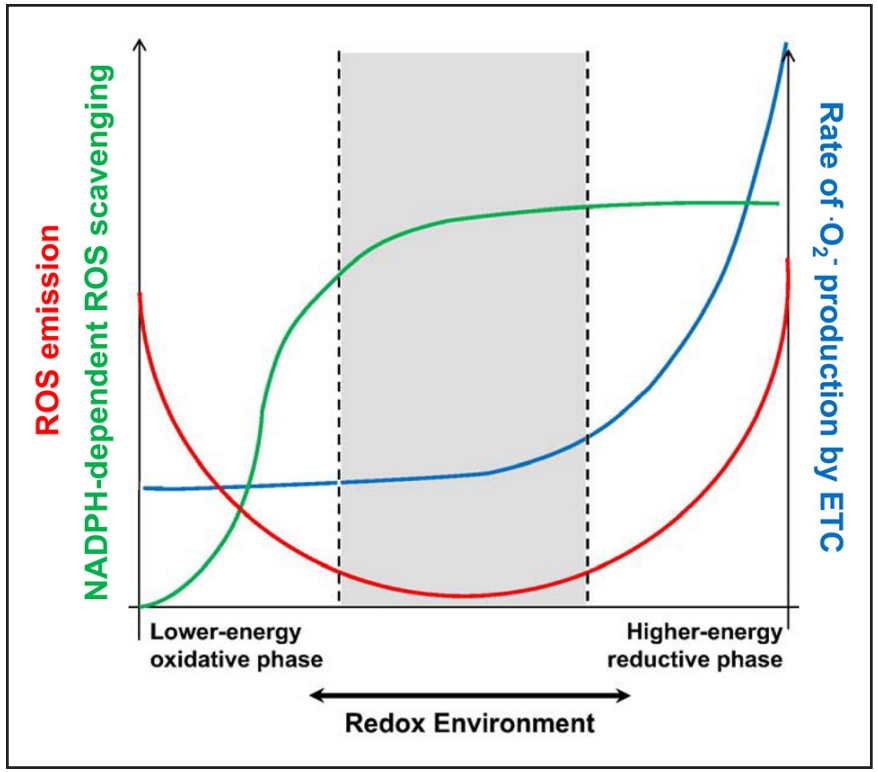


Figure 2. The redox-optimized reactive oxygen species (ROS) balance hypothesis. The plot illustrates that the redox environment in cardiac myocytes determines the net emission of ROS. The *x* axis denotes the redox state, from oxidized (**left**) to reduced (**right**), of NADH (nicotinamide adenine dinucleotide), $FADH_2$, NADPH (nicotinamide adenine dinucleotide phosphate), and the electron transport chain (ETC). Net ROS emission (red curve) is provoked at either reduced conditions (right side) when $\cdot O_2^-$ formation at the ETC is highest (blue curve), overwhelming the high NADPH-dependent ROS scavenging capacity (green curve). However, extreme oxidation gives rise to ROS emission because of dissipated antioxidative capacity. An optimum of energy production and ROS control exists in an intermediate redox state (gray shaded area), at which moderate $\cdot O_2^-$ production is controlled by sufficient antioxidative capacity. This redox state is the natural environment in working cardiac myocytes, in which a constant flux of electrons through the Krebs cycle matches oxidation of the ETC because of respiration. Adapted from Aon et al[29] with permission. Copyright ©2010, Elsevier.

Bertero and Maak Calcium signalling and reactive oxygen species in mitochondria *Circ Res* 2018

La parola al cardiochirurgo