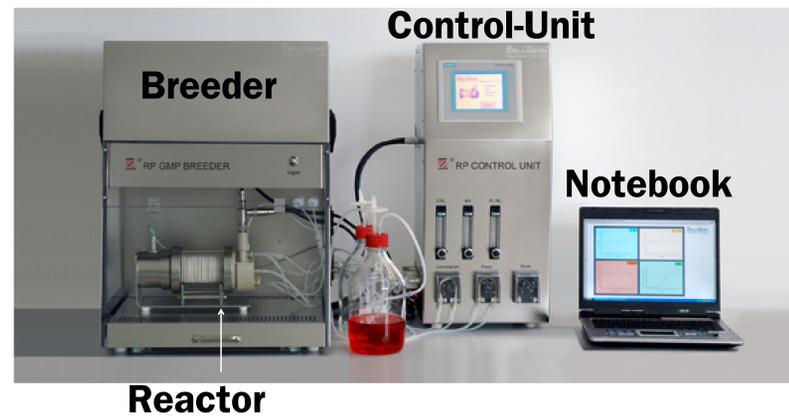


## Generation of Tumor-Antigen Specific T-Cells Under Highly Controlled Environmental Conditions by Utilization of a Novel, cGMP Compliant Cell Culture Reactor

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University of Erlangen-Nuremberg, Department of Internal Medicine 5 - Hematology/Oncology

### Z<sup>®</sup> RP Bioreactor



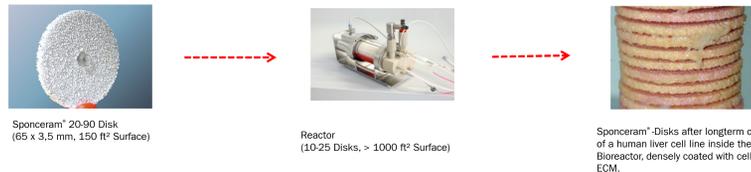
### The Z<sup>®</sup> RP System is fully compliant to:

- EC directives for production of Advanced Therapy Medical Products (ATMP): 2001/20/EC, 2001/81/EC, 2003/94/EC, 2004/23/EC, 2005/28/EC, 2006/17/EC, 2006/86/EC
- EC Regulations 726/2004/EC and 1394/2007/EC
- ICHQ10 Technical Requirements for Registration of Pharmaceuticals for Human Use
- EMA Guideline for production of medical products (MP) and ATMP Concept Paper on the Revision of the Guideline on Process Validation, May 2010
- EUDRALEX Vol. 4 Conformity with current Good Manufacturing Practices
- FDA requirements for cell-culturing systems for ATMP production Title 21 CFR part 210, part 211, part 600 and part 1271

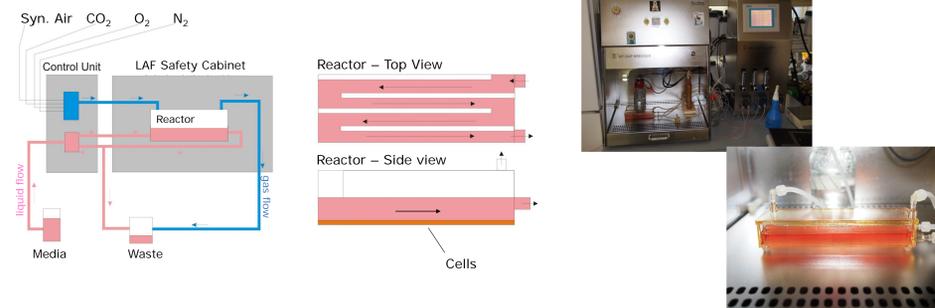
### Z<sup>®</sup> RP Bioreactor – Applications



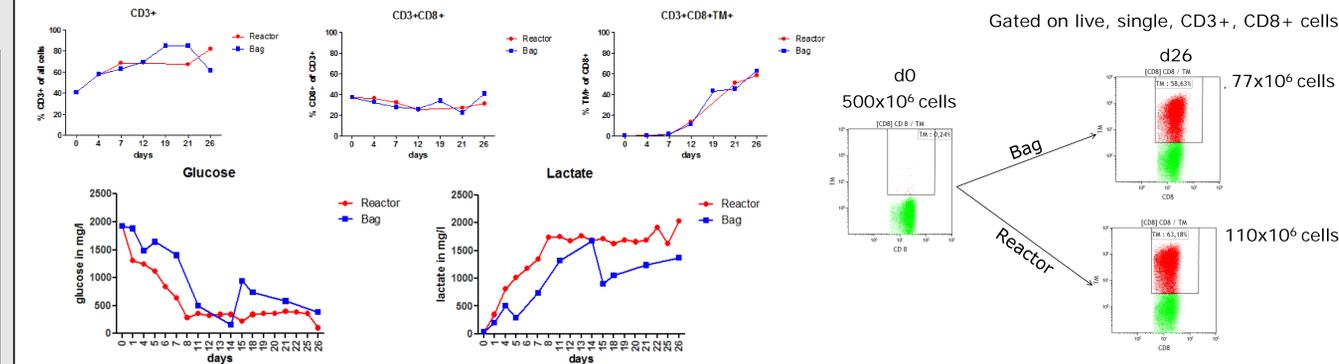
#### Adherent Cell Culture



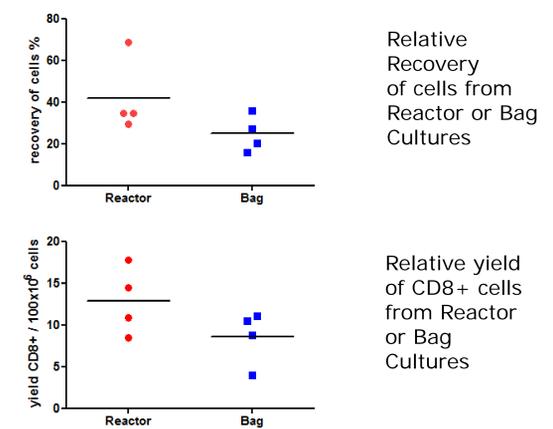
#### Suspension Cell Culture schematics



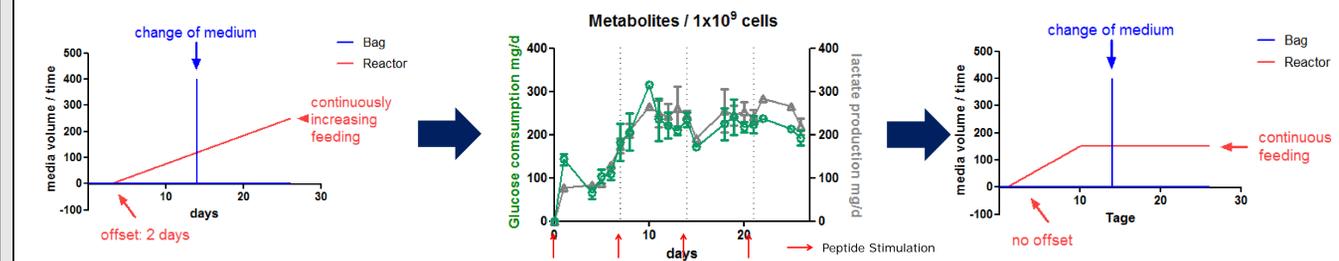
### Low Glucose / High Lactose Culture



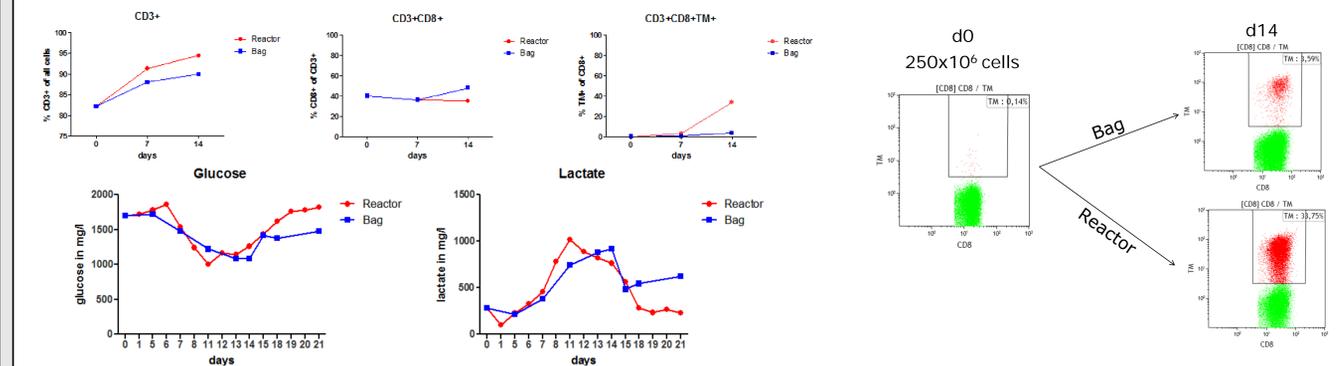
### Recovery and Yield



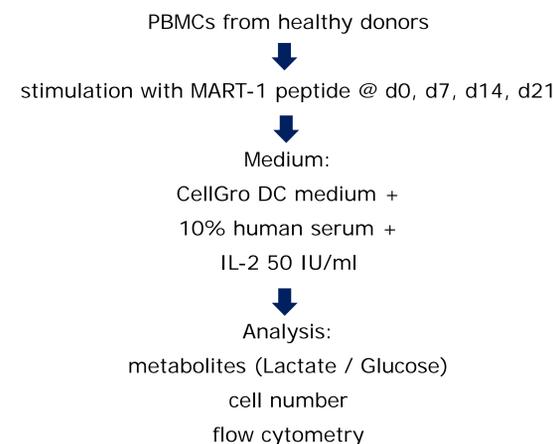
### Metabolism Analysis and Adaption of Feeding



### High Glucose / Low Lactose Culture



### Expansion of antigen-specific T-Cells

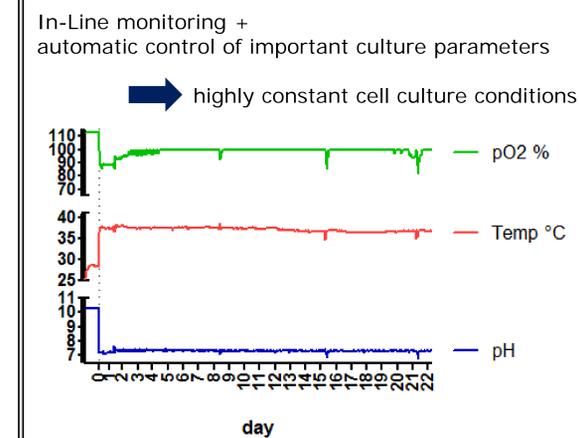


### Traditional Approach

**„Open“ Culture:**  
(cell culture dish or plate)  
+ highly established and characterized system  
+ ease of handling  
- No closed system  
➔ Not suitable for cGMP compliant production

**Bag Culture:**  
+ GMP compliant  
- discontinuously feeding  
- „Black Box“

### Reactor Culture



### Summary and Outlook

- Z<sup>®</sup>RP System is suitable for expansion of tumor-associated- antigen-specific T-Cells from complex PBMCs
  - Z<sup>®</sup>RP System is able to maintain extremely constant cell culture conditions for prolonged periods
  - Bag culture leads to high, spiking levels in lactate due to dis-continuous supply of cell culture medium
  - Reactor cultures show 68% higher recovery of CD3+ cells and 50% higher yield of CD8+ cells
- Outlook:
- further optimization of feeding
  - Normoxia vs. Hypoxia
  - expansion of pre-enriched T-Cells
  - culture for > 4 weeks