YAXINBIO

Warmly wellcome

http://www.yaxinbio.com

Enterprise Vision

- **Manufacturer of Animal Components Free recombinant proteins with *Eschericoli* system.**

  致力于生物医药用、无动物源性的重组蛋白和重组蛋白酶的研发和生产

- **Supplier of recombinant protein to Biopharmaceutical company.**

  为国际生物制药公司提供重组蛋白和重组酶。

- **Optimal individualized**

  为生物制药客户提供最优的个性化服务。

History of YaxinBio

- Established in 2008.
- In 2009, the first product, recombinant carboxypeptidase B was successful in market.
- In 2010, both rCPB and rTrypsin gained full success in Chinese market.

  exported rCPB and rTrypsin to Europe, India and Asia,got success in international market.

  2010年，重组羧肽酶B和重组胰蛋白酶在国内外市场获得成功。
- In 2012, move to a new office, Juke Biology Park.
- In 2012, Protein A, got success in market.

  2012年，重组蛋白A，在市场获得成功。
- In 2012, registed in NSF, ISO9001-2008 and fullfilled in Jul. 2013.
- 2012年，质量体系认证，2013获得认证证书，2014-2015，两次复审。
- In 2013, , RCPB and RPT, gained Shanghai hige-tech program .
- 2013年， RCPB and RPT申报并获得上海市高转项目。
- In 2014, Protein A, gained Shanghai hige-tech program

  2014，SPA申报并获得上海市高转项目。
- In 2015, applied for Shanghai hige-tech incorporation

  2015年，申报上海市高新技术企业。扩大生产。

主要产品

- 重组胰岛素生产用无动物源性重组酶

- (1). Recombinant Trypsin
- （重组胰蛋白酶）;
- (2). Recombinant Carboxypeptidase B
- （重组羧肽酶B）;
- (3). Recombinant Trypsin Inhibitor
- （重组胰蛋白酶抑制剂）

产品写进国内多家重组胰岛素生产和研发企业的SFDA申报资料中。

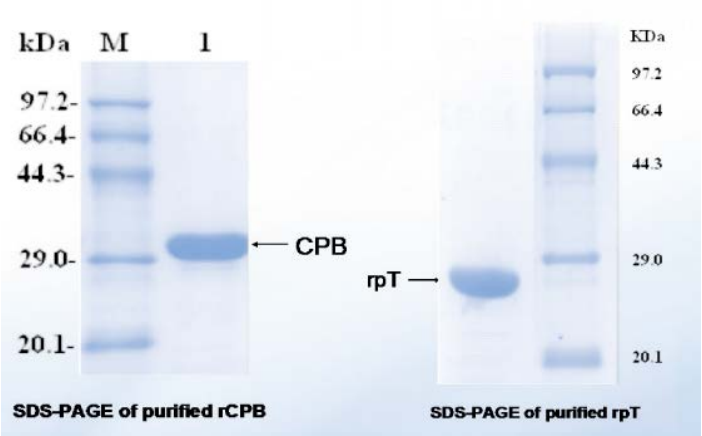
产品写进几家国际重组胰岛素生产企业申报政府批准，并正常使用

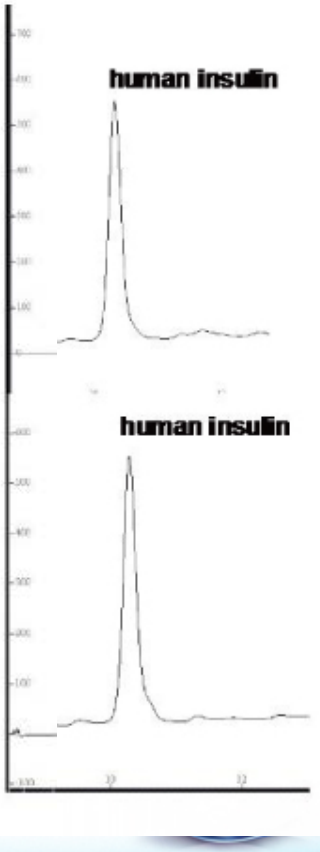
rTrypsin and rCPB

- **USE OF RECOMBINANT CARBOXYPEPTIDASE B AND RECOMBINANT TRYPSIN IN INSULIN MANUFACTURING**

无动物源性的重组羧肽酶B和重组胰蛋白酶应用于重组胰岛素生产过程中。

ACF rh-Insulin and analogues





主要产品

重组胰蛋白酶—符合USP2014

- 重组胰蛋白酶的系列产品：

(1) Recombinant trypsin (human 2,PRSS II)
重组人胰蛋白酶I

(2) Recombinant trypsin (human 1,PRSS I)
重组人胰蛋白酶II

(3) Recombinant trypsin (porcine, RPT)
重组猪胰蛋白酶

(4) Recombinant trypsin (bovine, RBT)
重组牛胰蛋白酶

重组生产，无动物源性，彻底改善我国疫苗企业生产的动物源性问题。从一个重要途径上避免了人畜共患病的传播。

应用于疫苗生产，重组蛋白生产、免疫治疗等领域。

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Products List

Cat. No.	Product Name	Function	Application	Charaters	Package
RCPB01	Recombinant Carboxypeptidase B	catalyzes lysine, arginine and histidine from C-terminal of polypeptides.	r-insulin production, antibody C-termial identification, sequencing, etc	Special Activity (unit/mg) NLT 170	10mg,100mg,1gr, or bulk.
RPT0201	Recombinant Trypsine (porcine)	endoproteinase, hydrolyzes polypeptides at the carboxyl side of lysine and arginine, comply with USP 2014	r-insulin production, biopharmaceutical process, cell culture	Special Activity (USPU/mg) NLT 3800	10mg,100mg,1gr, or bulk.
SRT0202	Recombinant Trypsine Sequence	endoproteinase, hydrolyzes polypeptides at the carboxyl side of lysine and arginine	peptide mapping, fingerprinting, and sequence analysis	Special Activity (USPU/mg) NLT 6000	20μg, 100μg, 1mg
RHT03	Recombinant Trypsine (human)	endoproteinase, hydrolyzes polypeptides at the carboxyl side of lysine and arginine, comply with USP 2014	biopharmaceutical process,cell culture,cell dissociation, human cell therapy, stem cell, etc.	Special Activity (USPU/mg) NLT 3800	10mg,100mg,1gr, or bulk.
RTS04	Recombinant Trypsine Solution	endoproteinase,hydrolyzes polypeptides at the carboxyl side of lysine and arginine, comply with USP 2014	cell culture,cell dissociation, biopharmaceutical process,etc.	Activity 2000 BAEE unit/ml	10ml,100ml,1L or bulk
RSPA05	Recombinant Protein A	binds to most human and mouse IgG subclasses. can be coupled to solid separation media to purify polyclonal or monoclonal IgG antibodies, can be coupled to a variety of molecules (such as fluorescent molecules, enzyme markers, biotin, colloidal gold and radioactive markers) used in antibody test in the process of Western-blot, ELISA or immunohistochemical tests, ect.		Purity NLT 95%	10mg,100mg,1gr, or bulk.
RLA06	Recombinant Lipase A	catalyzes the hydrolysis of fats and oils with excellent enantioselectivity.(1) Hydrolysis of trans-3-(4-methoxyphenyl) glycidic acid methyl ester [(±)-MPGM] (-)-MPGM.(2) Hydrolysis of (±)-naproxen methyl ester to produce (-)-naproxen. (3)Catalysis of ester substitution reaction, etc.		Activity 1000 unit/gr, 2000 unit/gr	1gr, 10gr, or bulk.
REK08	Enterokinase (EK)	cleaves lysine C-terminal preceded by four aspartic acids: Asp-Asp-Asp-Asp-Lys	delete extra N-terminal fusion protein to gain full recombinant protein	Activity (unit/μl) 10-50	100unit, 500unit, 1ku, or bulk.
RPK09	Recombinant proteinase K	endopeptidase. digest native proteins, thereby inactivating enzymes	used in the process of DNA extraction,etc.	Activity NLT 30	10mg,100mg,1gr, or bulk.
RCT10	Recombinant Chymotrypsine	endoproteinase, hydrolyzes polypeptides at the carboxyl side of aromatic amino acids: Tyr, Phe and Trp.	protein digests for peptide mapping or protein identification by peptide mass fingerprinting or MS/MS spectral matching.	Special Activity (unit/mg) NLT 1000	10mg,100mg or bulk.
V813	V8 (Endoproteinase Glu-C)	endoproteinase, cleaves peptide bonds C-terminal to Glu and Asp	insulin analysis, peptide mapping, fingerprinting, and sequence analysis	Activity (unit/mg) 20	1 unit, 50 μg, 2mg.

主要产品

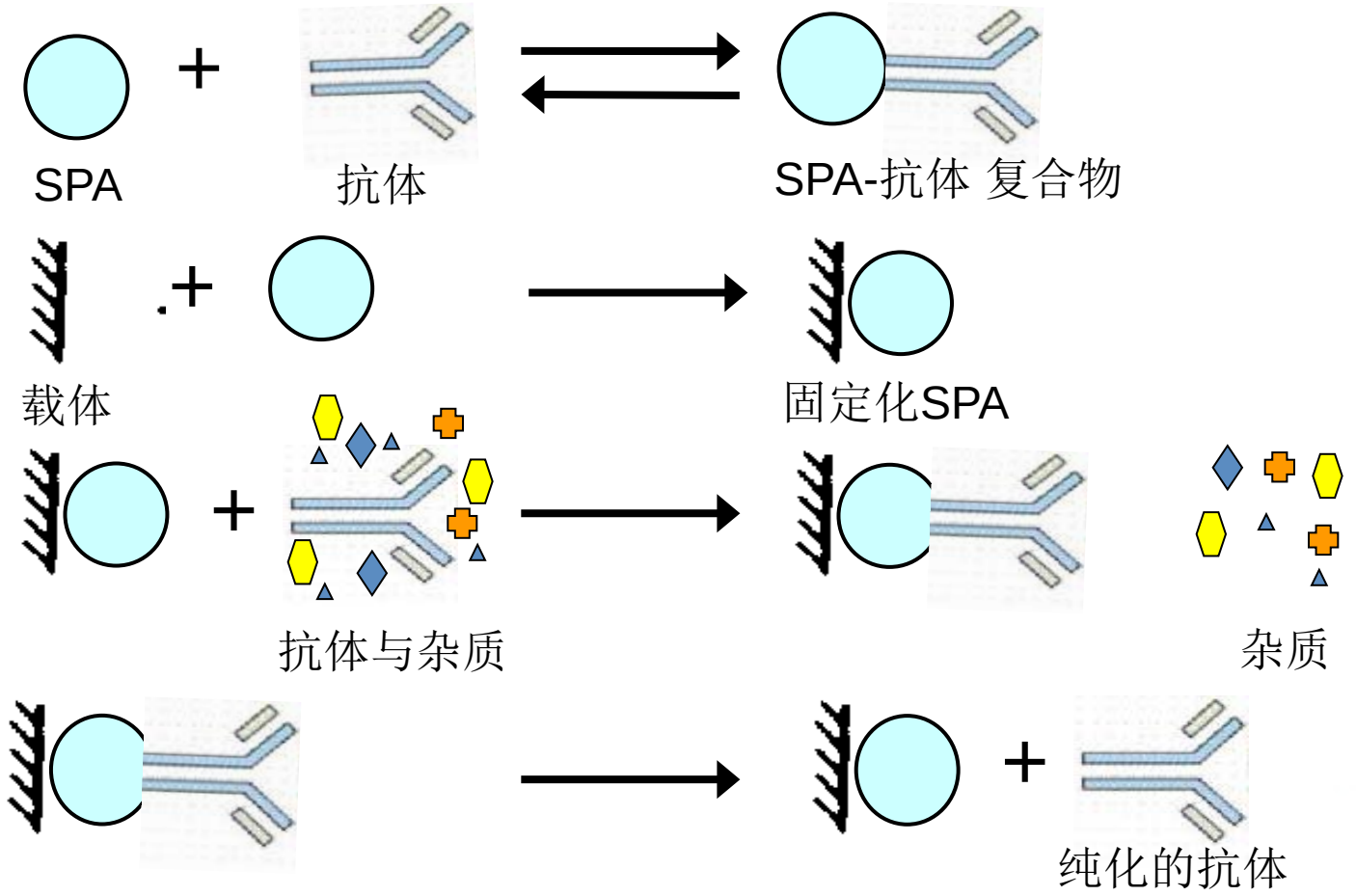
重组蛋白A

原理

1 偶联

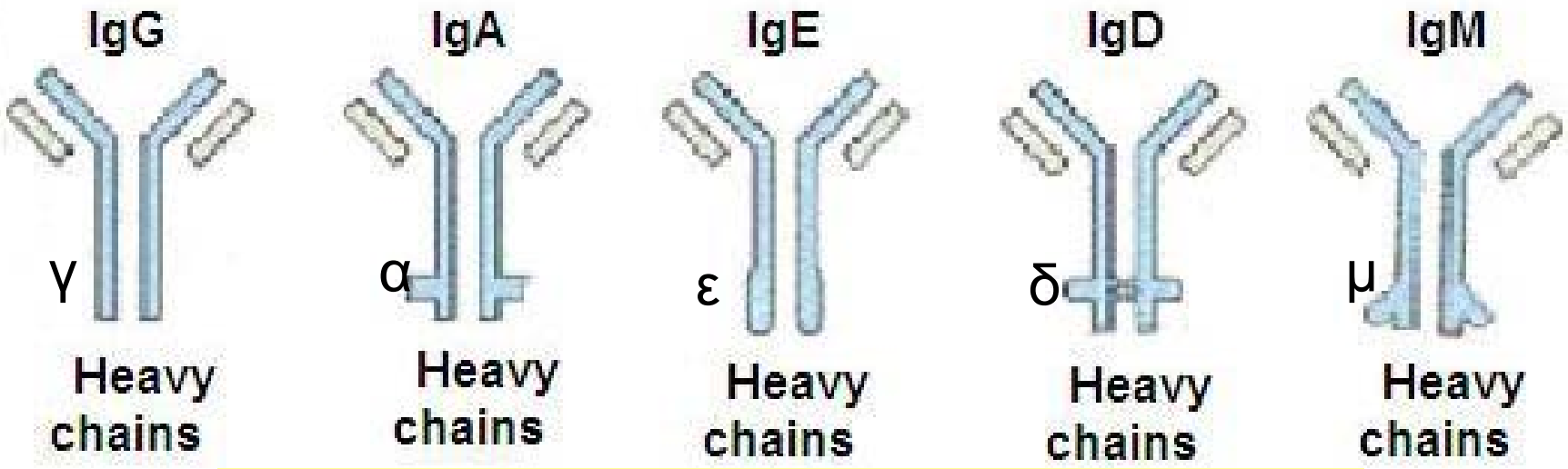
2 吸附

3 纯化

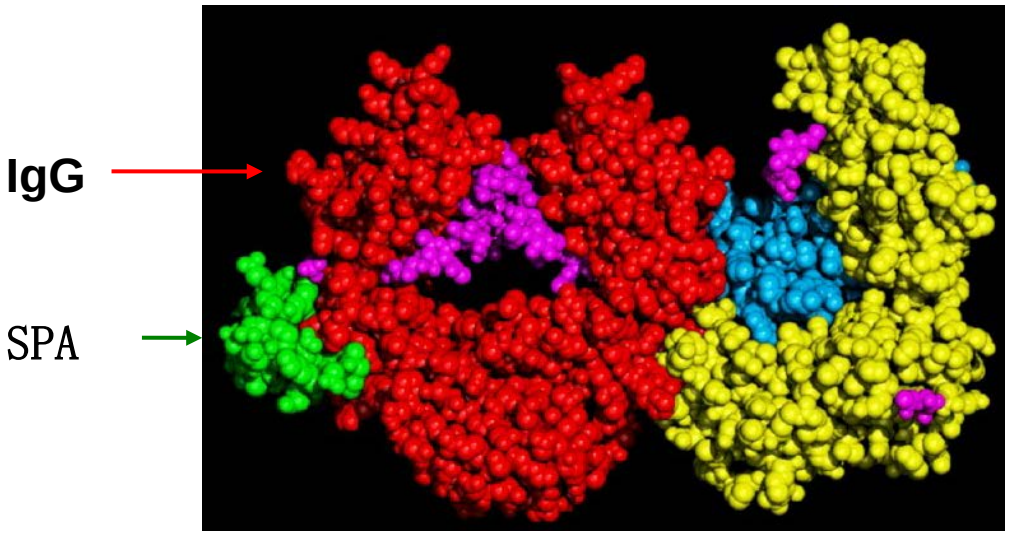


替代进口，节约抗体生产成本一半。

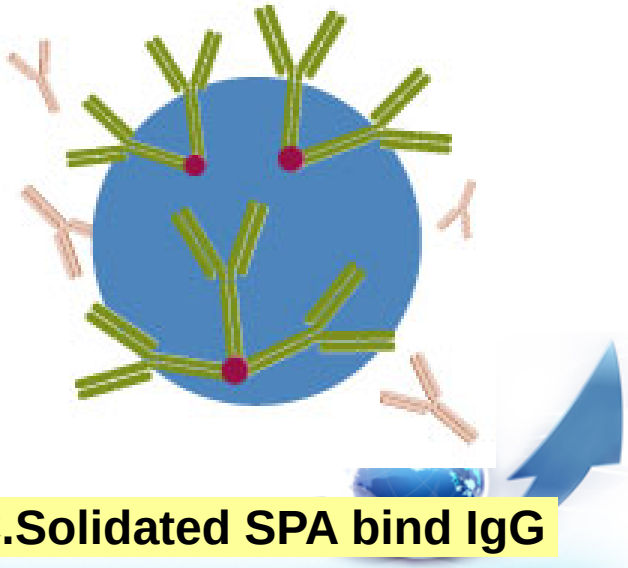
Protein A



A. Sketch of structure of Different kinds of antibodies



B. Specific binding between SPA and IgG Fc fraction



C.Solidated SPA bind IgG

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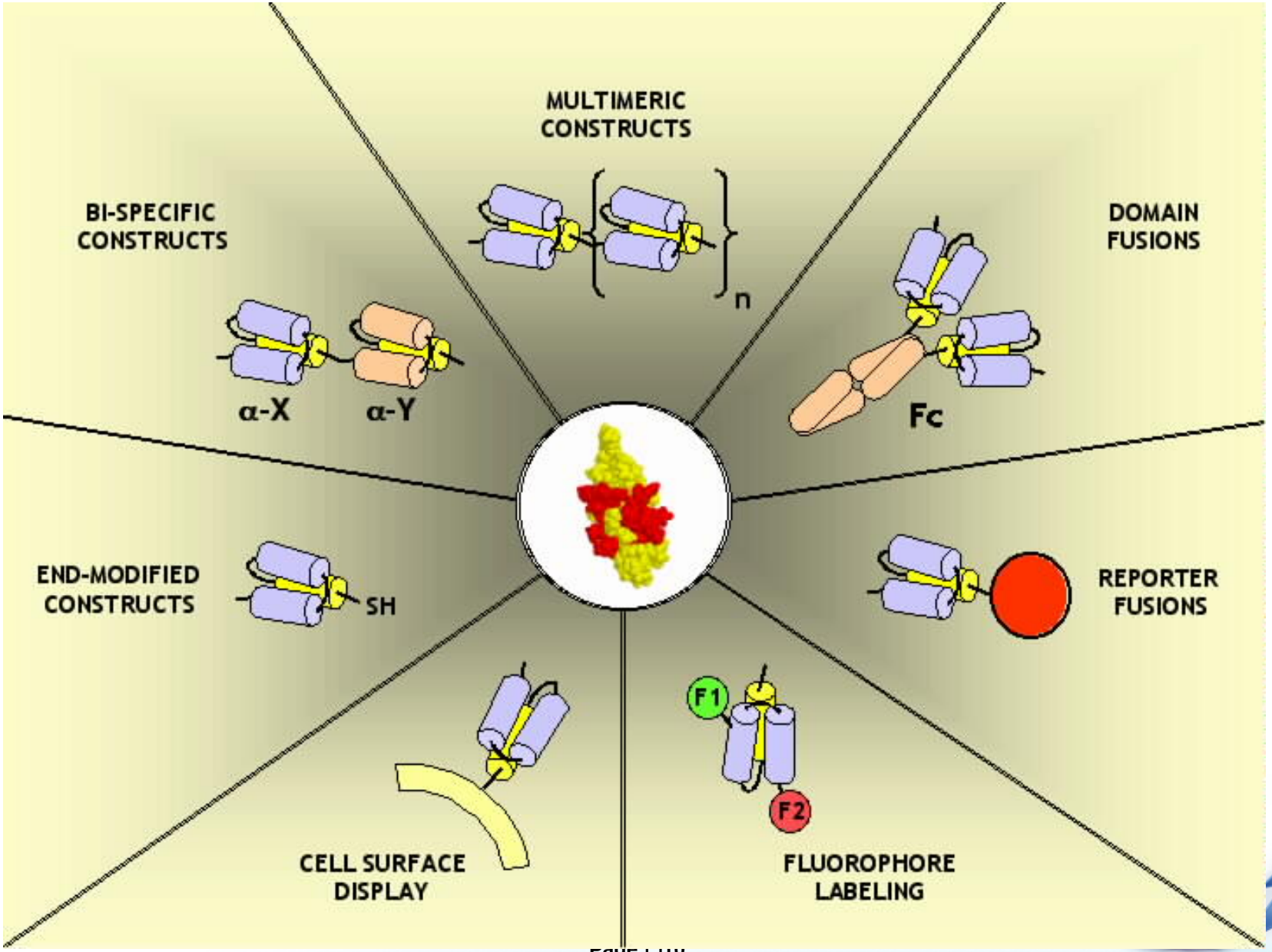
Usage field of SPA

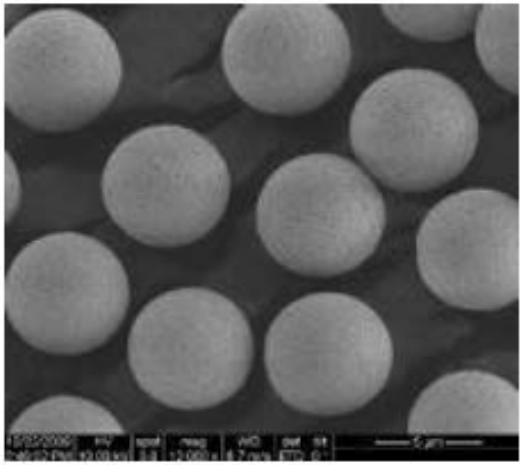


SPA affinity resins

Particle size comparison of Protein A affinity resins

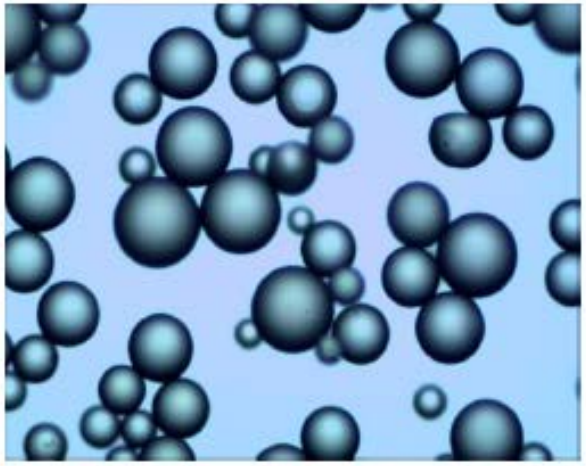
Sepromax A40 Plus

PS-DVB ; 40um monodisperse



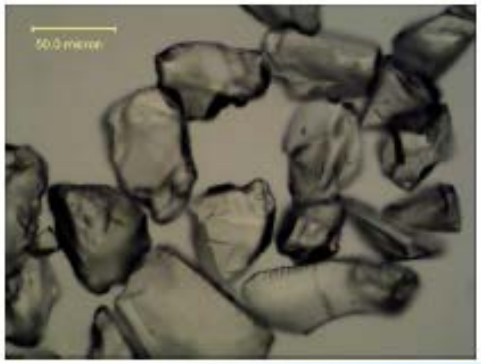
MabSelect SuRe

Agarose ; 40-130um Mean 85um



ProSep Ultra Plus

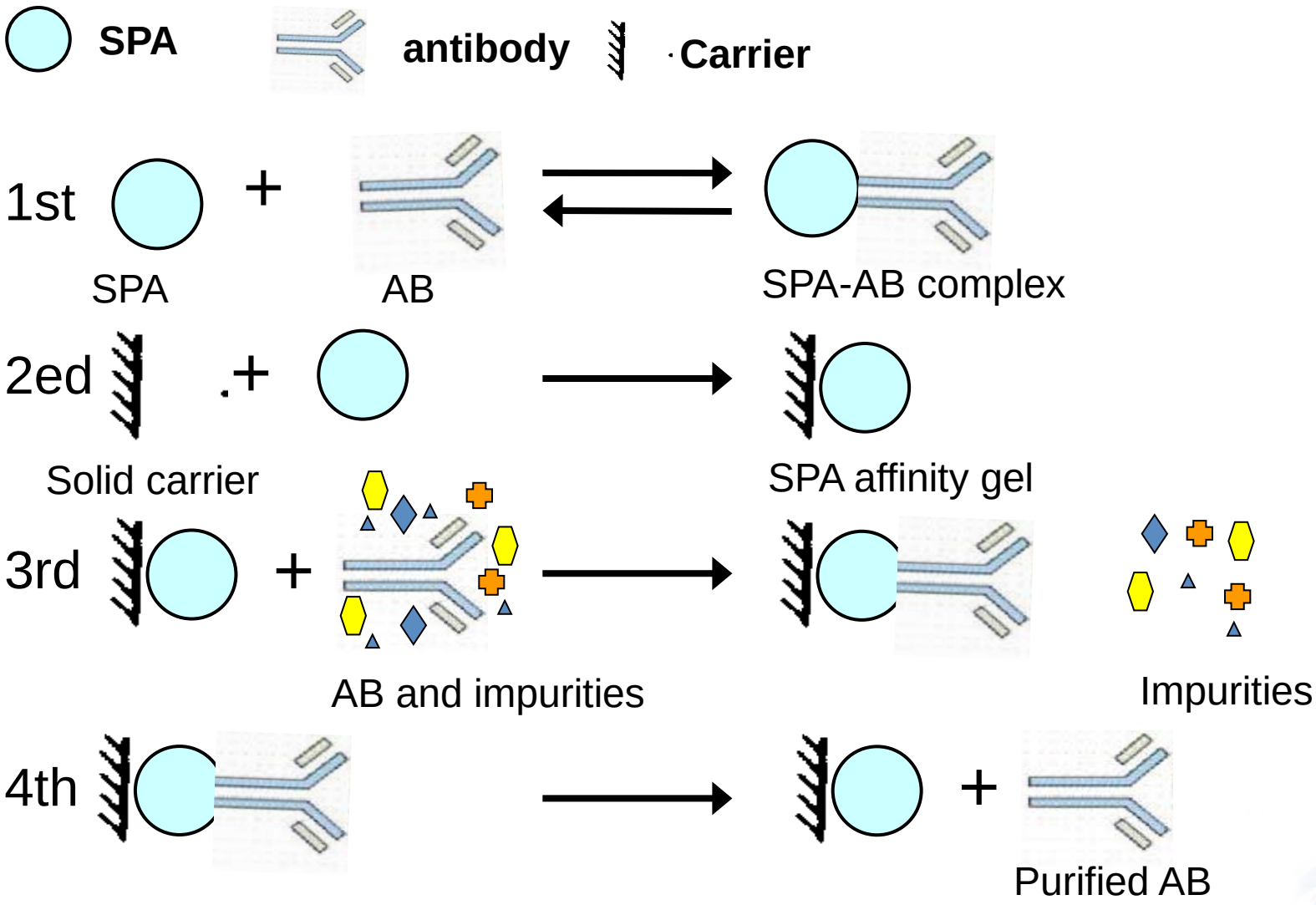
CPG ; 40-130um Mean 65um

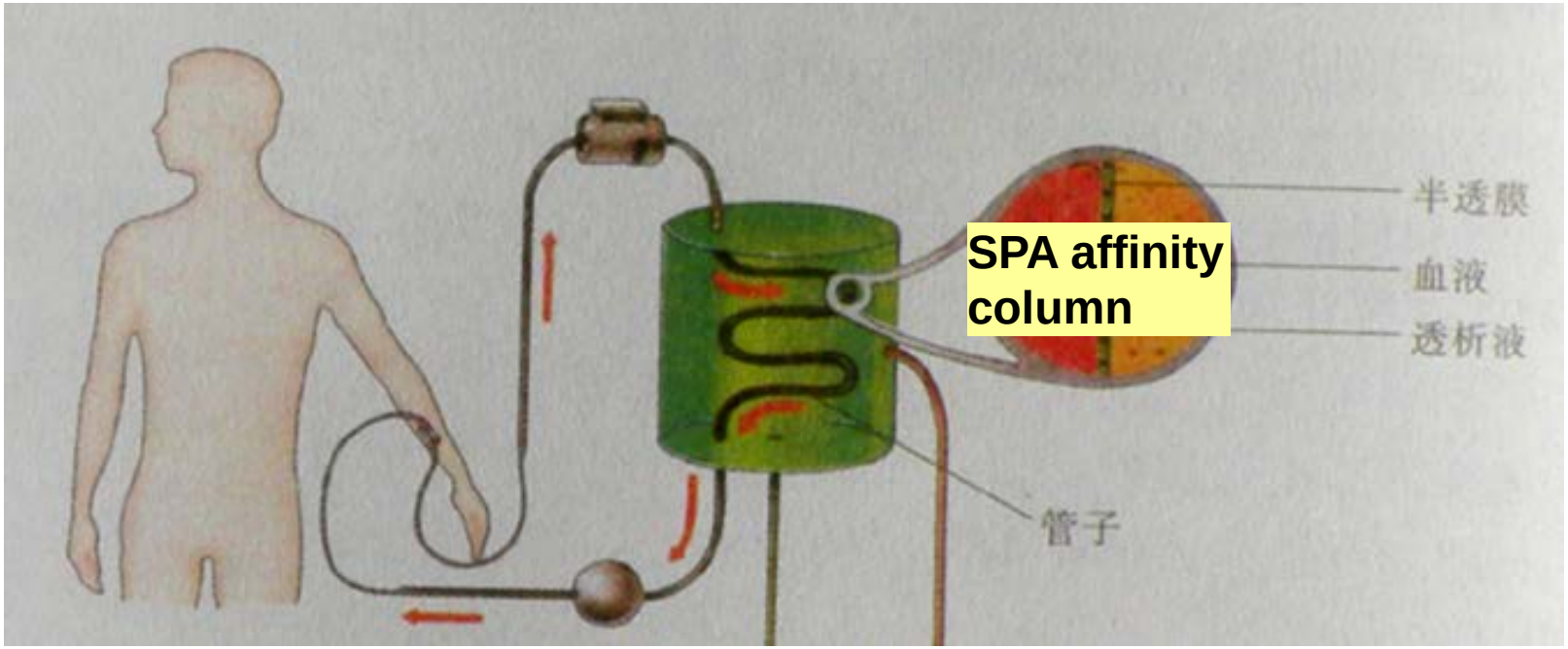


POROS MabCapture A

PS-DVB ; 30-70um Mean 45um

Principle of SPA affinity gel to purify antibody



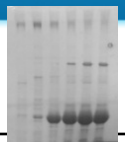


In vitro, SPA affinity column absorb extra antibodies produced and existed in immunity patient blood, it is one kind of immunity therapy.

SPA 亲和胶治疗免疫性肾病，通过吸附患者体内多余的抗体。

YAXINBIO R-Protein A production Process

Recombinant strain E. Coli



Fermentation

centrifugation

cell

lysis

centrifugation

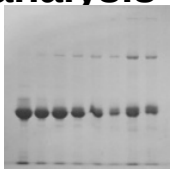
supernatant

Ultrafiltration

Chromatography purification 1

Chromatography purification 2

analysis



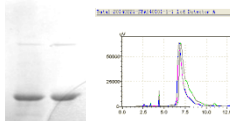
concentration

Sterile Filtration

Lyophilization

Sterile Chamber

Packaging



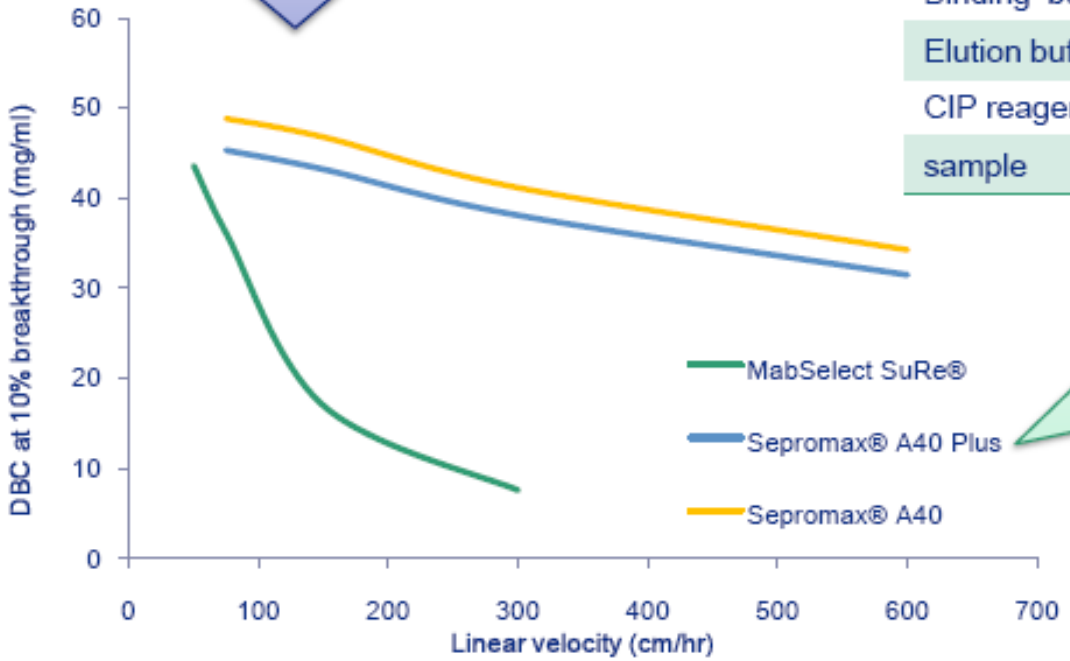
Examination

Protein A affinity resin

Dynamic Binding Capacity

Pr-A affinity resin	Column size	Column volume
Sepromax® A40	ID 4.6×50 mm	0.83 ml
Sepromax® A40 Plus	ID 4.6×50 mm	0.83 ml
MabSelect SuRe®	HiTrap 7.0×25 mm	1.0 ml

DBC at different flow rate



Test conditions	
System	AKTA® Purifier10
Binding buffer	20 mM PB , 0.15 M NaCl , pH 7.4
Elution buffer	0.1 M Gly-HCl , pH 2.5
CIP reagent	0.5 M NaOH
sample	1.0 mg/ml hIgG

Based on same matrix, the DBC curves of A40 and A40 Plus show nearly same variation trend. Contrary to MabSelect SuRe, the DBC of Sepromax A40 Plus doesn't decrease significantly with the increase of flow rate.

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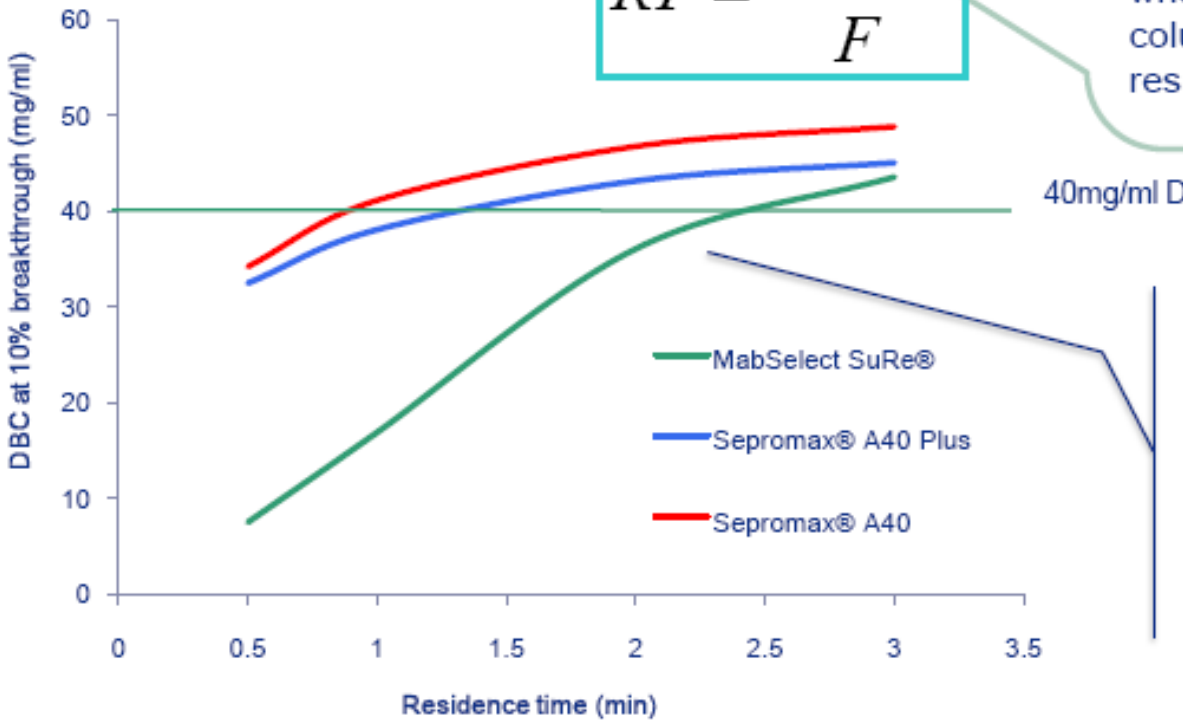
Protein A affinity resin

Dynamic Binding Capacity

Residence time vs. DBC

$$RT = \frac{H \times 60}{F}$$

Due to column size difference between Sepromax A40 Plus and MabSelect SuRe, we suggest to compare base on residence time using the formula RT=H*60/F where F is flow rate (ml/min), H is column height(cm), RT is residence time(min).



Example:
To obtain 40mg/ml DBC, RT of Sepromax A40 Plus is 1.2min,and MabSelect SuRe is 2.4min.
Under the 10cm-column height, flow rate of Sepromax A40 Plus is 500cm/h, MabSelect SuRe is 250cm/h

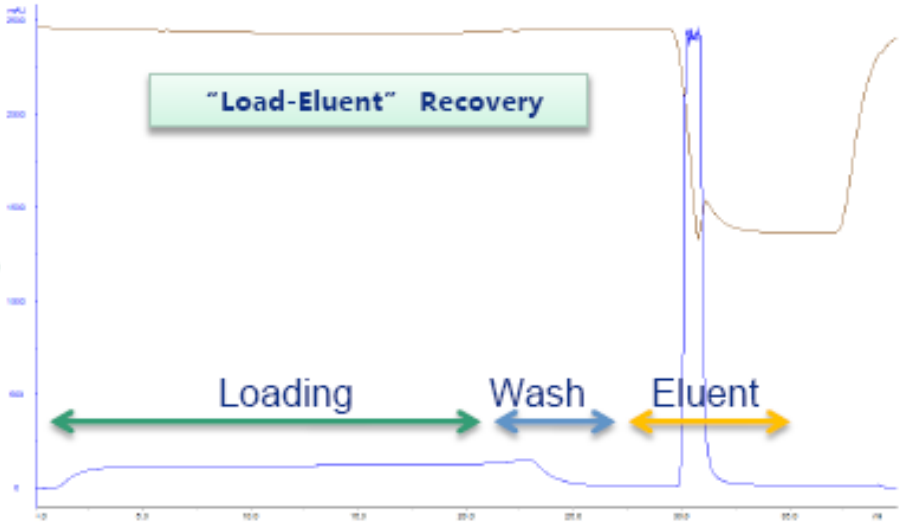
Choose Sepromax A40 Plus, gain high efficiency

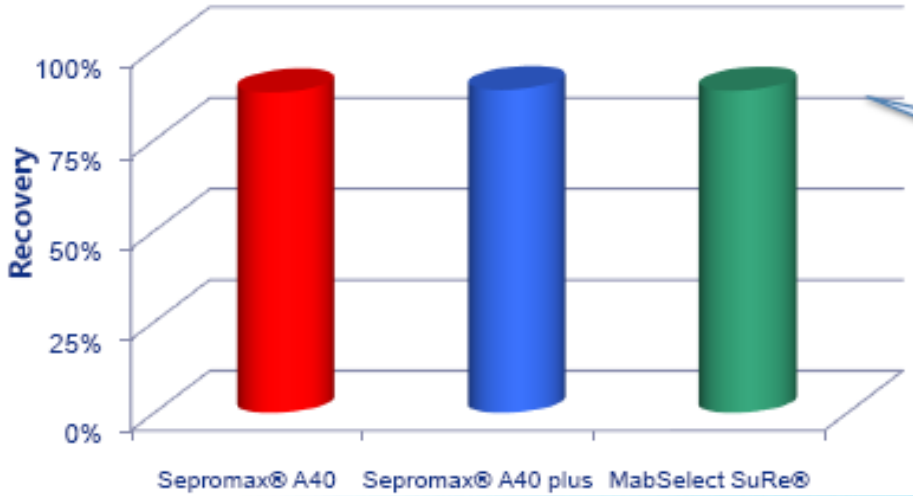
Protein A affinity resin

Recovery test

"Load-Eluent" Recovery

With polymer substrate, Sepromax A40 Plus showed excellent hydrophilic and very low non-specific interaction as polysaccharide media(MabSelect SuRe).





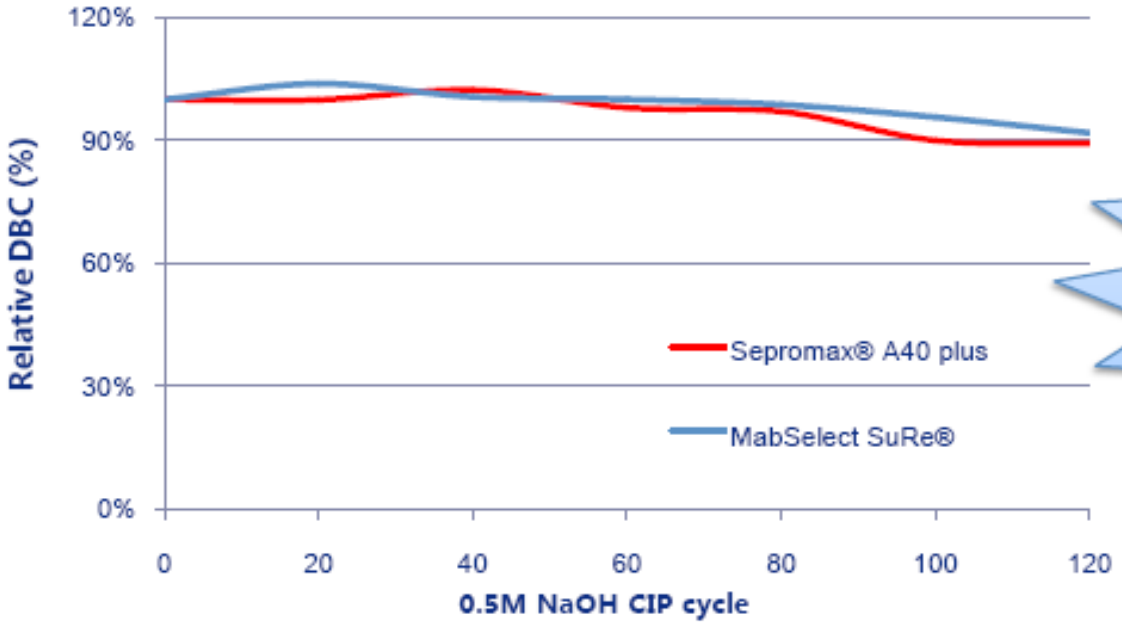
There's no significant difference on "load-elution" recovery rate between Sepromax A40 plus and MabSelect SuRe!

Protein A affinity resin

Alkaline stability study

Alkaline stability study

CIP condition: 0.5M NaOH, contact time 10 min each cycle, DBC test after every 20 cycles.



No difference!

Protein A affinity resin

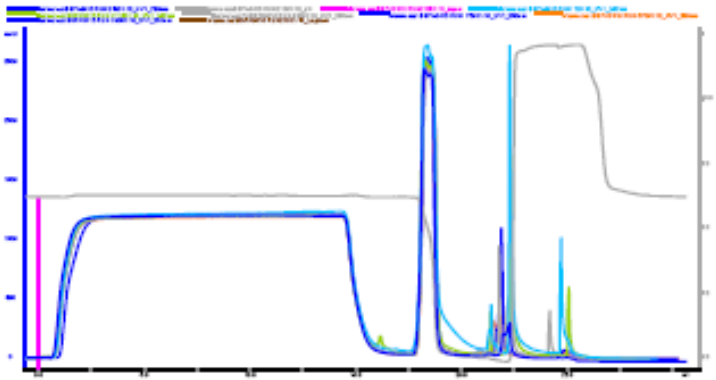
Lifetime study

150-cycle lifetime test

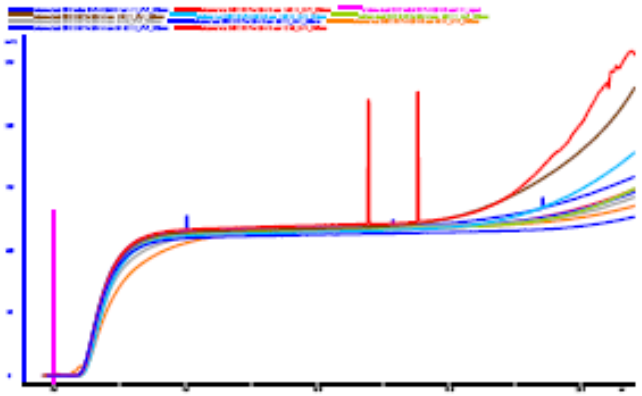
A 150 loading and elution cycles study with CIP in every cycle revealed that Sepromax A40 Plus possessed excellent durability under harsh conditions.

步骤	溶液组成	体积或时间
平衡	20 mM PB，0.15M NaCl，pH7.4	5CV
上样	1mg/ml hIgG+ BSA/Lysozyme	RT=0.6min，50%DBC
冲洗	20 mM PB，0.15M NaCl，pH7.4	5CV
洗脱	0.1M Gly-HCl，pH3.0	5CV
CIP	0.1M NaOH	4CV=15min

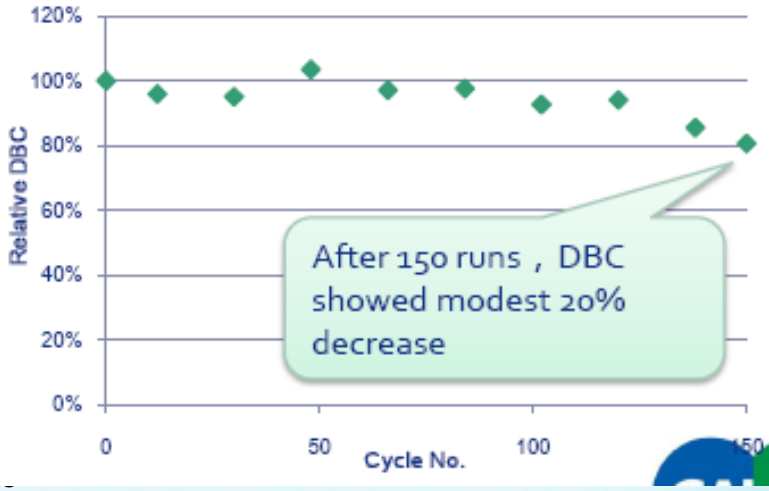
Overlay of chromatograms from runs in lifetime test



Overlay of chromatograms of DBC tests



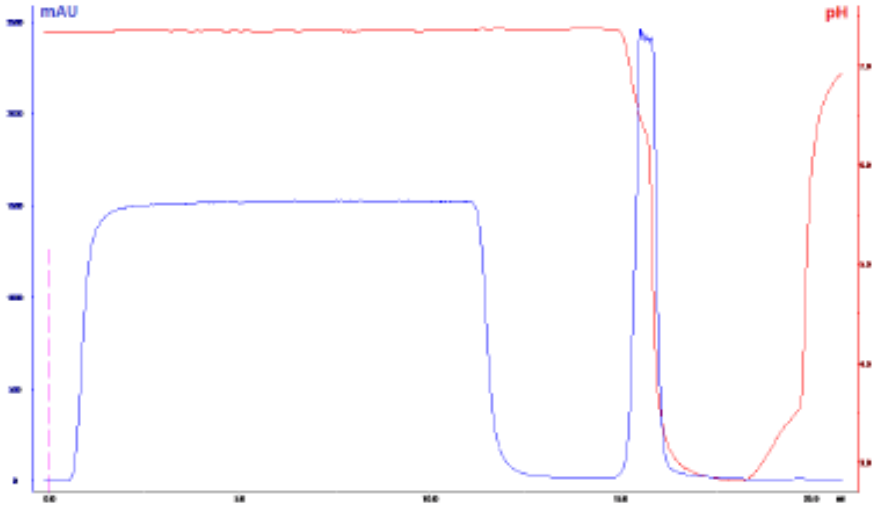
Relative DBC of Sepromax® A40 Plus during 150 lifetime cycles



Protein A affinity resin

Application

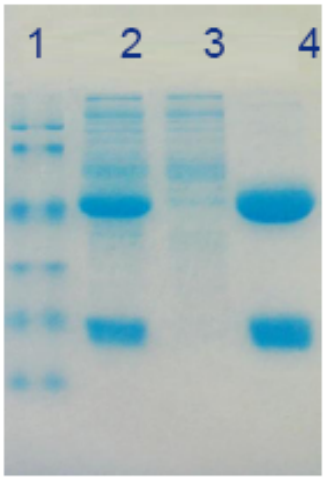
Purification of Human IgG from human serum



- Column: 4.6 ID×50 mm L
- Sample: Diluted Human Serum
- Loading buffer: 20 mM pH 7.5 PB with 0.15 M NaCl
- Elution: 0.1 M pH2.5 Glycine HCl

Purification of hIgG from Human Serum using Sepromax® A40 Plus.

An example of purification of human IgG is shown above. Human IgG was obtained from diluted human serum on a Sepromax® A40 column. Non-reduced and reduced SDS-PAGE gel electrophoresis results are shown right.



Lane:
1. Marker
2. Diluted human serum
3. Flow-through
4. Elution

HCP removal efficiency test

Impurity removal test – host cell protein (HCP)

- **Material and Method**

  Host protein CHO testing kit, manufacturer: Cygnus, Cat. No.: CM015

  ELISA method : put standards、samples、selected impurities、internal standard into marked holes (96 holes) to get incubated. Then put anti-CHO protein antibodies to go through color development. Finally use ELISA reader determine 450 nm light absorption values.

- **Results**

  Generate the standard curve, calculate the internal standard recovery rate, and then determine the HCP content using the following equation:

  HCP content(ng/mg)=$R_{TS}/(C_{ST}/d_{TS})$ 或 HCP(%)=$[R_{TS}\times10^{-6}/(C_{ST}/d_{TS})]\times100$

  Where :R_{TS} is the detected ELISA sample HCP conc. (ng/mL) , C_{ST} sample conc. (mg/mL) , d_{TS} the dilution factor

Protein A affinity resin

Removal test of HCP

❖ Impurity removal: test- host cell proteins (HCP)

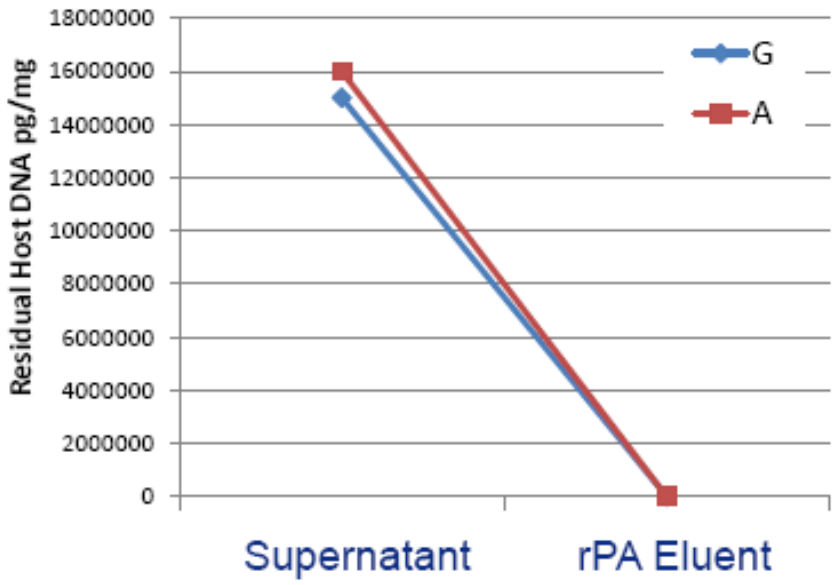
HCP(ng/mg)	Sepromax A40 Plus	MabSelect SuRe
supernatant	1754.3	1716.5
elution	1.9	4.5
Purification factor	9.2×10^2	3.8×10^2

Conclusion： Sepromax A40 Plus is a little bit better than MabSelect SuRe at the removal of residual host cell proteins.

Protein A affinity resin

DNA removal efficiency test

- Impurity removal: test- host DNA



rDNA(pg/mg)	Sepromax A40 Plus	MabSelect SuRe
supernatant	1.5×10^{7}	1.6×10^{7}
elution	154.4	431.3
DNA Purification factor	9.7×10^{4}	3.7×10^{4}

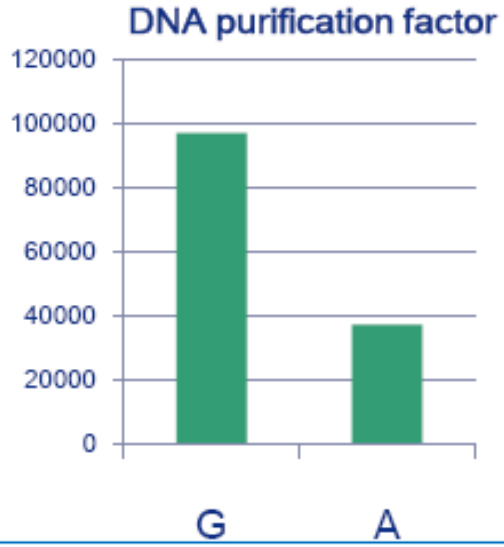


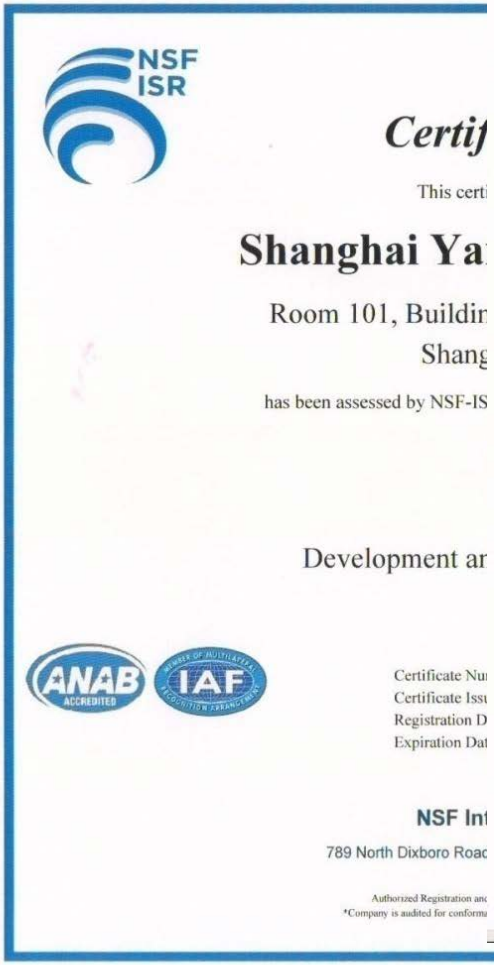
Figure on the right shows that both Sepromax A40 rPA material and product from company A possess ability to remove DNA. The two lines showed identical trend due to large lowering factors. Yet, Figure on the right shows that DNA lowering factor before and after the affinity chromatography. Sepromax A40 rPA material has higher ability in removing CHO cell DNA than the product from company A.

自主知识产权


证书号第1077877号
发明专利
发明名称：一种高稳定性的重组胰蛋白酶的
发明人：冯矗;赵致
专利号：ZL 2009 1 0055493.8
专利申请日：2009年07月28日
专利权人：上海雅心生物技术有限公司
授权公告日：2012年11月14日
局长
证书号第1077867号
发明专利
发明名称：一种高稳定性的重组羧肽酶B的
发明人：冯矗;赵致
专利号：ZL 2009 1 0055492.3
专利申请日：2009年07月28日
专利权人：上海雅心生物技术有限公司
授权公告日：2012年11月14日
局长
证书号第1077877号
发明专利
发明名称：一种高稳定性的重组胰蛋白酶的生产
发明人：冯矗;赵致
专利号：ZL 2009 1 0055493.8
专利申请日：2009年07月28日
专利权人：上海雅心生物技术有限公司
授权公告日：2012年11月14日
局长
证书号第1714571号
发明专利证书
发明名称：高稳定性的具抗体结合能力的重组蛋白A及其生产
发明人：李素霞;赵致;冯矗
专利号：ZL 2010 1 0614100.5
专利申请日：2010年12月30日
专利权人：上海雅心生物技术有限公司
授权公告日：2015年07月01日
局长
申长雨
2015年07月01日

YAXINBIO

质量体系认证



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上海市高新技术转化项目

证　书

项目编号：201309537　项目等级：A　技术贡献系数：0.90

项目名称：重组羧肽酶 B

项目单位：上海雅心生物技

该项目经审定，认定为

有效期至2021年 11 月。

上海市

证　书

项目编号：201309538　项目等级：A　技术贡献系数：0.90

项目名称：重组胰蛋白酶

项目单位：上海雅心生物技术有限

该项目经审定，认定为上海市

有效期至2021年 11 月。

上海市高新技术

2013 年

证　书

项目编号：201409443　项目等级：B　技术贡献系数：0.86

项目名称：重组蛋白 A

项目单位：上海雅心生物技术有限公司

该项目经审定，认定为上海市高新技术成果转化项目，

有效期至 2019 年 9 月。

上海市高新技术成果转化项目认定办公室

2014 年 9 月 30 日

Marketing oversea

Marketing China

Thank you