Ólafur Friðjónsson

Capacity for novel product development of sea cucumber carbohydrates

HOLOSUSTAIN project workshop

Online 8.10.2020

INITIATING A NORTH ATLANTIC NETWORK
ON SUSTAINABLE HOLOTHURIAN TECHNOLOGY AND INNOVATION

Sea cucumbers arround Iceland

- **Sea cucumber are found all arround Iceland in substantial quantities**
- **16 differented species have been observed in the see arround Iceland**
- **The largest species which is mainly caught is *Cucumaria frondosa* , "Brimbrjótur"**
- **The sea cucumbers grow slowly, it takes them arround 6 years to grow and reach marketing size**

Icelandic sea cucumber products

Capsules with *Cucumaria frondosa* extracts

Arctic Star sea cucumber capsules contain more than 50 types of nutrients, high in collagen, 18 types of amino acids, taurine, chondroitin sulphate, polypeptides, calsium, phosphor, iron, iodine, zink, selen,vanadium, manganese, vitamines B1, B2, B3, B5 and more

***Cucumaria frondosa* extakt** rich in collagen, zink, iodine og iron. Contains bioactive chondroitin sulphate and saponin

Research and development activities at Matís have a strong focus on the blue bioeconomy.

Holosustain objective:

Incorporate a searchable data library as Intranet access, specifically focused on sea cucumber chemical, nutritional and metabolic potential, as a tool for the discovery of novel, potential health-related products, and applications.

marine drugs

MDF

Review

Northern Sea Cucumber (*Cucumaria frondosa*): A Potential Candidate for Functional Food, Nutraceutical, and Pharmaceutical Sector

Abul Hossain [1], Deepika Dave [1,2,*] and Fereidoon Shahidi [1,*]

1 Department of Biochemistry, Memorial University of Newfoundland, St. John's, NL A1B 3X9, Canada; abulh@mun.ca

2 Marine Bioprocessing Facility, Centre of Aquaculture and Seafood Development, Fisheries and Marine Institute, Memorial University of Newfoundland, St. John's, NL A1C 5R3, Canada

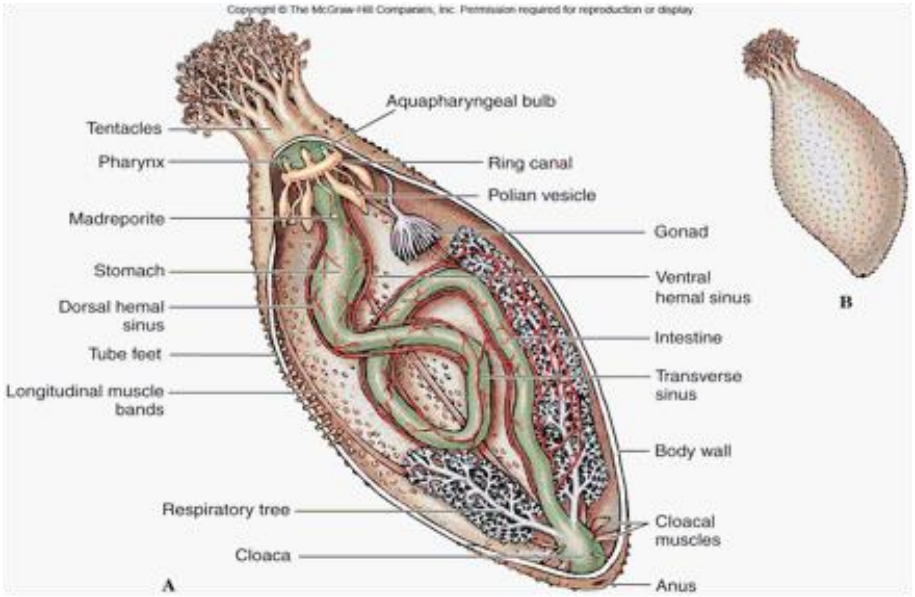
* Correspondence: Deepika.Dave@mi.mun.ca (D.D.); fshahidi@mun.ca (F.S.)

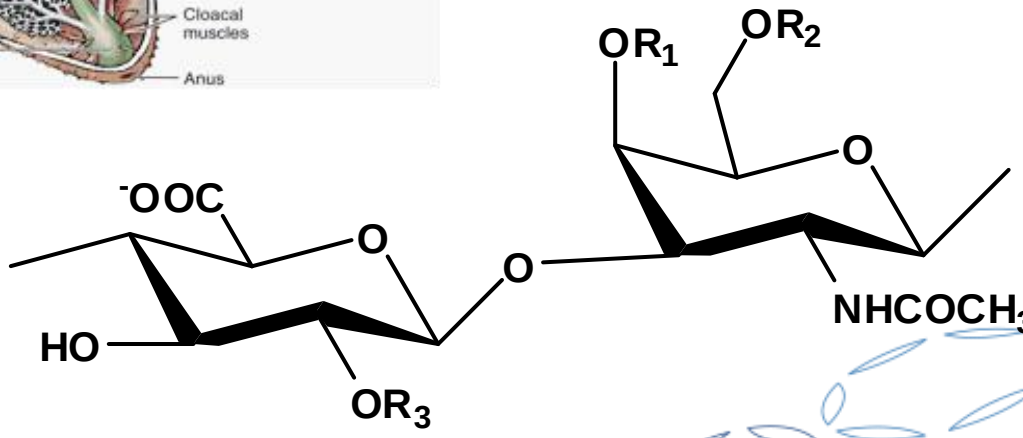
Received: 1 May 2020; Accepted: 20 May 2020; Published: 22 May 2020

check upda

matis

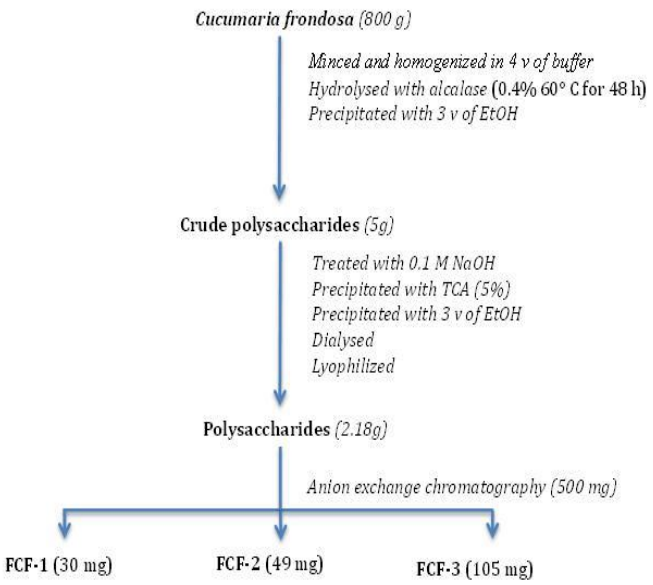
Isolation, structural characterization and bioactivity studies of sulfated sea cucumber polysaccharides

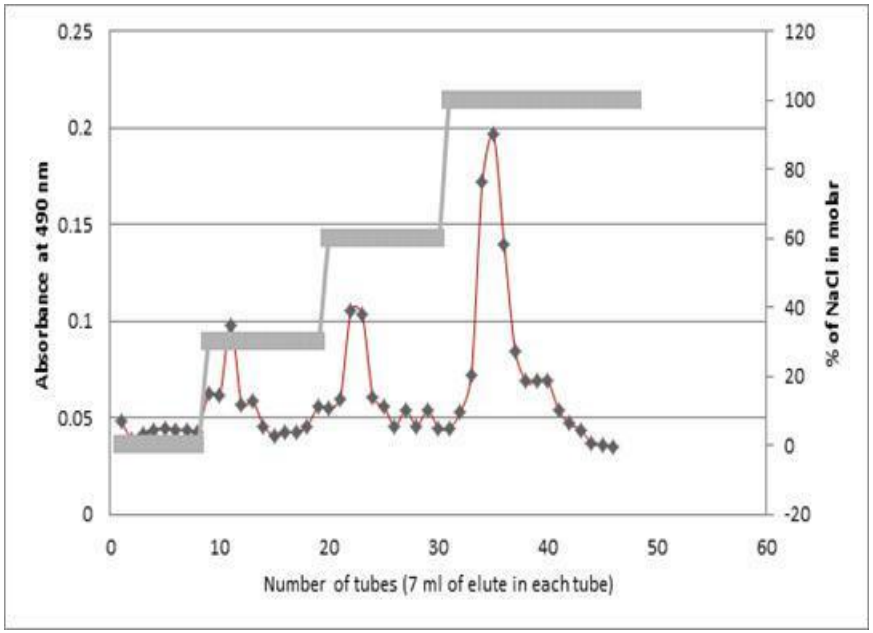




Chondroitin sulfate

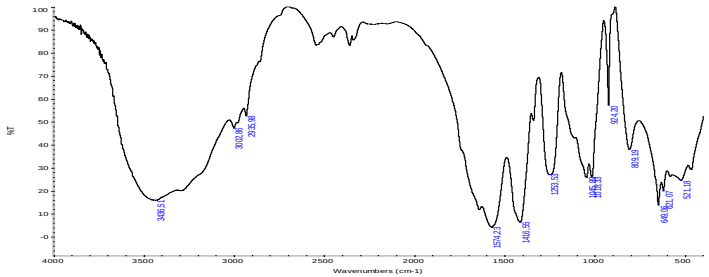
Extraction and fractionation of sulphated polysaccharides from *C. frondosa*

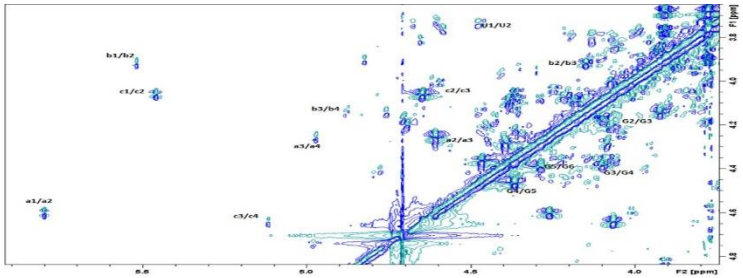


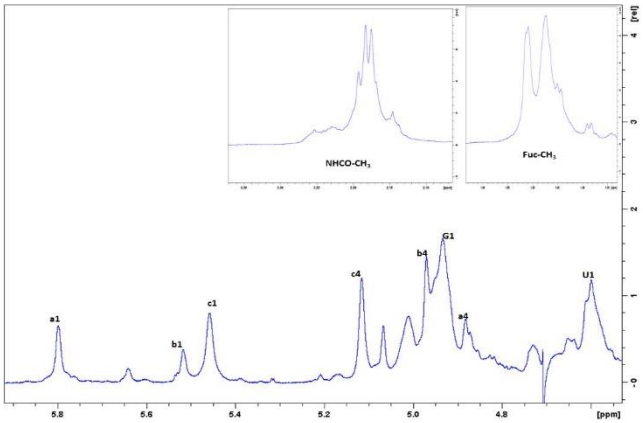


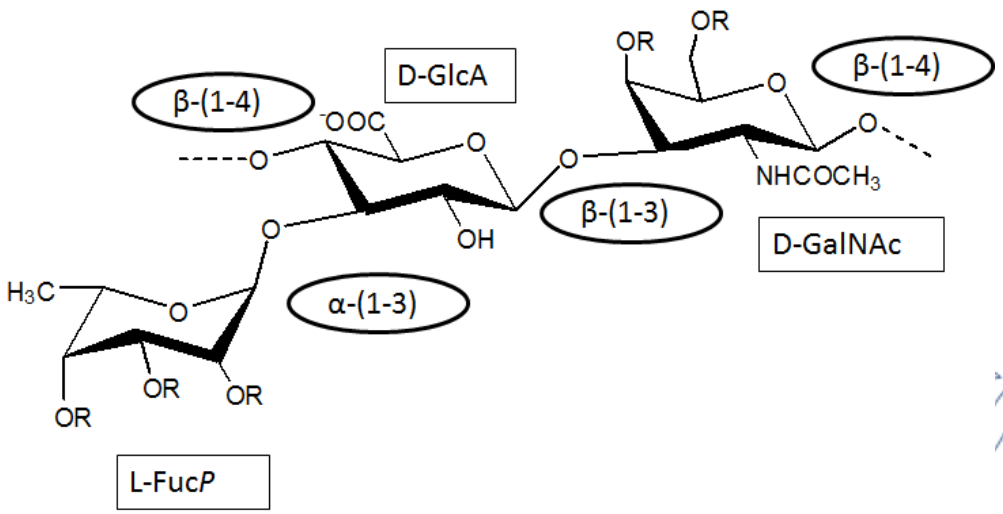
Polysaccharides	Mr (kDa)	Protein (%)	Lipid (%)	Sulfate (%)	Molar ratio %							
					NANA	GalNAc	GlcA	Fuc	Man	Glc	Gal	GlcNAc
FCF-1	>2000	2	<0.1	26.3	40.0	3.3	-	8.6	13.3	8.0	12.1	12.3
FCF-2	30	6	<0.1	32.4	19.8	2.8	6.32	30.5	-	34.0	2.9	1.5
FCF-3	270	0	<0.1	34.5	12.6	28.8	16.8	34.6	-	-	3.7	2.0

Structural analysis of FCF-3









Bioactivity studies

- Antioxidant activity
- Imunomodulating activity
- Antidiabetic activity

Focus of this study

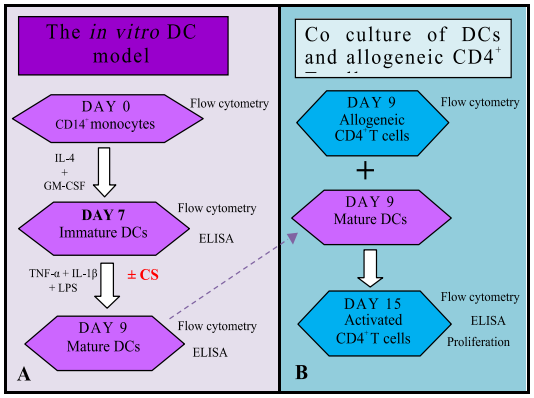
- Antithrombotic
- Anticoagulant
- Anticancer
- Anti-inflammatory
- Antimicrobial actitivy
- Anti-hyperglycemic
- Prebiotic activity

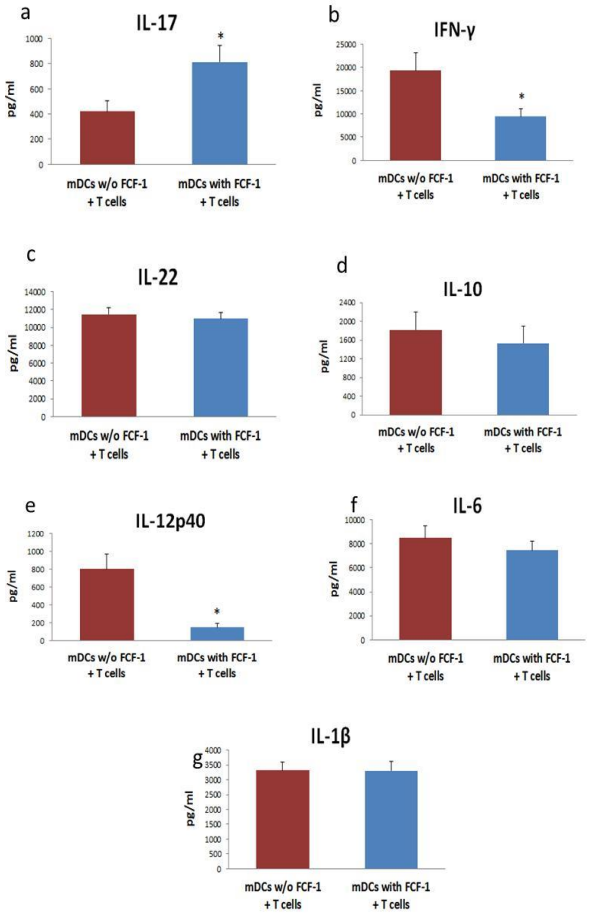
Immunomodulatory activity

- Investigated using a dendric cell model

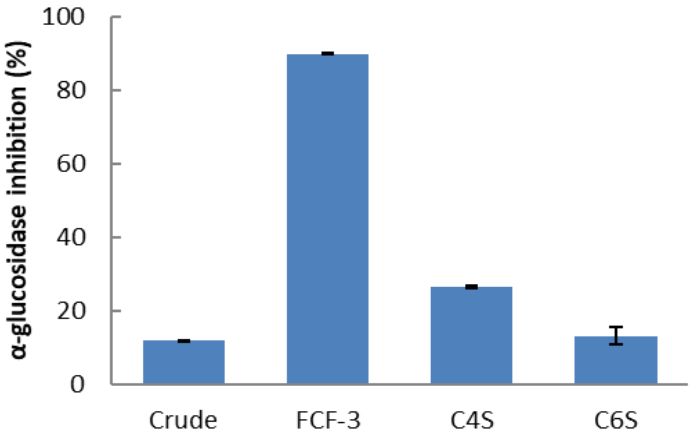
- **Fraction 1 (FCF1) showed significant immunomodulating activity**
- The high molecular weight FCF1, containing mannose and substantial amount of N-acetyl-neuraminic acid affects the maturation DCs and their availability to activate T cells.
- The figure shows secretion levels of cytokines following cell maturation with and with out **FCF1.**

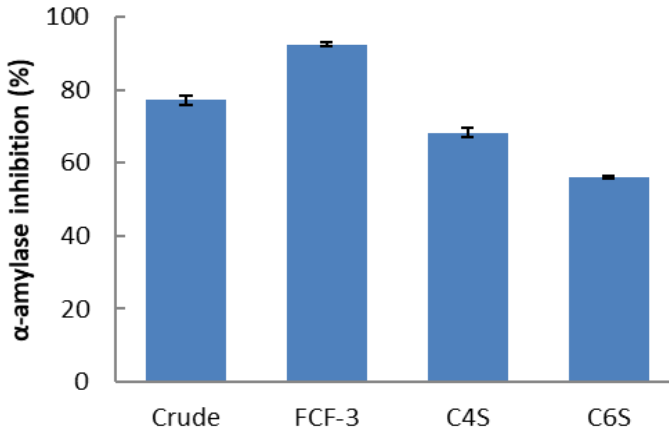
- Beneficial in the fight against extracellular infections and in limiting various chronic inflammatory responses





Anti-diabetic activity





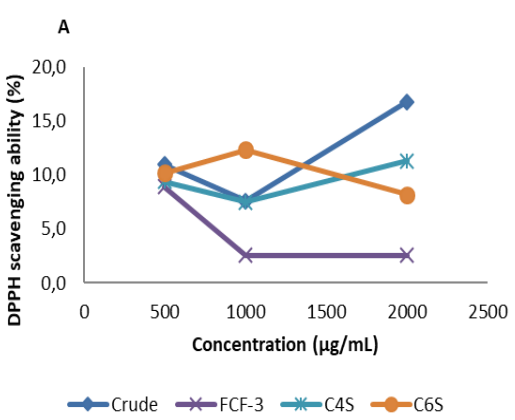
	Crude	FCF-3	C4S	C6S	Acarbose
α-amylase IC_{50} (μg/mL)	8.0	6.9	19.2	35.5	2.2
α-glucosidase IC_{50} (μg/mL)	-	20	-	-	2550

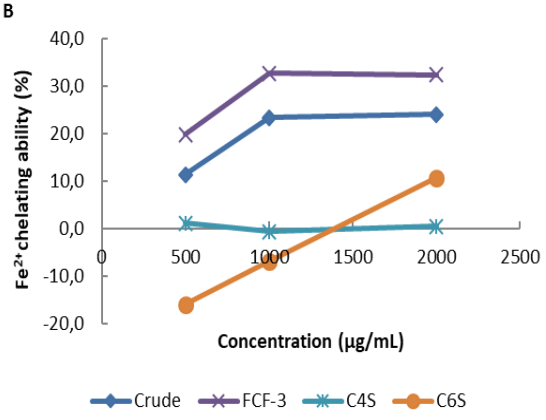
- FCF-3 with fucosylated chondroitin sulfate showed significant activity of starch enzymes
- Potential as an anti-diabetic drug used for the prevention and diabetes type 2 and its complications.

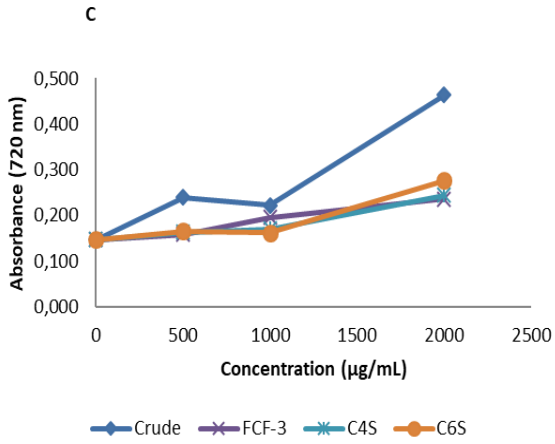
Anti-oxidant Activity

Three different assays:

- DPPH radical scavenging activities
- Ferrous chelating ability
- Reducing power assay







Sea cucumber chondroitin sulfate is a moderate antioxidant according to ferrous chelating ability and reducing power competence attributed to its high sulfate content

Conclusions of these studies

- Three types of sulfated polysaccharides has been isolated from body wall of Atlantic sea cucumber *Cucumaria frondosa*
- These polysaccharides are differing in physiological properties
- FCF-1 (and FCF-2) shows potential immunomodulating activity
- FCF-3 (chondroitin sulfate) is strong inhibitor of α-glucosidase, and moderate inhibitor of α-amylase – anti-diabetic activity
- Antioxidant activity assay revealed that FCF-3 (chondroitin sulfate) is moderate antioxidant compound, and the activity is attributed to its high sulfate content

Biologically active compounds of Atlantic sea cucumber and their functions Hossain et al Mar. Drugs 2020, 18, 274

- Collagen
- Glycosides (Saponins)
- Phenolic compounds
- Cerebrosides
- Proteins/amino acids
- Vitamins and minerals
- Fatty acids (omega-3)

Table 3. Biologically active compounds of Atlantic sea cucumber and their functions.

Bioactives	Body Parts	Biological and Medicinal Effects	Extraction and Isolation Method	References
Fucosylated chondroitin sulfate	Body wall	Antithrombotic, anticoagulant, anticancer, anti-inflammatory, antitumor, antidiabetic, anti-osteoarthritis, alleviates inflammation, alleviates pain, and improve immune system	Enzymatic (papain/ Alcalase) hydrolysis followed by precipitation (cetylpyridinium chloride/ ethanol/ sodium hydroxide/ tricholoracetic acid)	[57,93,99]
Collagen	Body wall	Antihypertension, antiaging, anti-wrinkle, alleviates skin problems, and wound healing	A divalent cation chelator (EDTA) followed by extraction in water	[79,80]
glycosides (saponins)	Body wall	Antibacterial, antifungal, antiviral, antitumor, anticancer, antiangiogenic, and photo-protective	Isopropyl alcohol/ water extraction and refluxing with chloroform/ methanol/ethanol	[83,100,101]
Fucoidan	Body wall	Anticoagulant, antibacterial, antiaging, anti-hyperglycemic, lowering blood glucose level, and photo-protective	Hydrolysis with papain and precipitation with cetylpyridinium chloride	[58,70]
Phenolic compounds	Body wall, tentacles, and viscera	Antioxidants and antibacterial	Solvent extraction (methanol), water, organic solvent (ethyl acetate) and a mixture of water/ miscible organic solvent (acetonitrile)	[16,54]
Cerebrosides	Body wall	Anticancer, anti-inflammatory, and anti-adipogenic activity	Solvent extraction (65% ethanol) and isolated by High-performance liquid chromatography (HPLC), extracted by chloroform/ methanol using high speed counter-current chromatography	[19,102,103]
Amino acid	Body wall, tentacles, and viscera	Anti-fatigue, repairing tissue, nutritional storage, and wound healing	Reversed phase HPLC	[54,55]
Protein (bioactive peptide)	Body wall	Antimicrobial	Fractionated utilizing ammonium sulfate precipitation and analyzed by size exclusion chromatography	[32]
Vitamin and minerals	Body wall, tentacles, and viscera	Cosmeceutical properties, promote healthy growth and metabolism, lower the blood sugar level	Association of Official Analytical Chemists (AOAC)-and inductively coupled plasma mass spectrometry (ICP-MS)	[55,93]
Omega-3 (EPA)	Body wall, tentacles, and viscera	Anti-hyperglycemic, decrease cholesterol, and protect the heart	Solvent extraction (methanol: chloroform: water) and analyzed by gas chromatography (GC)/ HPLC	[50,54,55,104]

Can these compounds be extracted and purified on a commercial scale in a cost-effective way for the health market?

- Production of extracted, purified compounds to increase volume activity and valorization
- Yield of sulfated body wall sugars isolated at laboratory scale: 0,1% of the body wall feed stock

- Methods and protocols need to be optimized and up scaled to yield refined marketable products based on the body wall bioactive saccharides.
- The production of such products needs to be sustainable and cost effective
- At the same time, the rest raw material also needs to be processed e.g. in a cascaded manner to optimize utilization of the different bioactive components because the sea cucumbers are a valuable and a limited source

Thank you ！