Strain code	Species	Class	Phylum	Habitat	Cell size (µm)
LAFW02	Cf. *Chloromonas* sp.	Chlorophyceae	Chlorophyta	Freshwater	10-20
LACW42	*Amphidinium* sp.	Dinophyceae	Miozoa	Marine	15-30
LACW24	*Stauroneis* sp.	Bacillariophyceae	Bacillariophyta	Marine	10-20
LACW34	*Phaeothamnion* sp.	Phaeothamniophyceae	Ochrophyta	Marine	10-50
DMGFW08	*Ankistrodesmus* sp.	Chlorophyceae	Chlorophyta	Freshwater	20-40
DMGFW31	*Pediastrum* sp.	Chlorophyceae	Chlorophyta	Freshwater	40-100
APSW11MA	*Brachiomonas* sp.	Chlorophyceae	Chlorophyta	Marine	5-15
DMGFW21	*Kirchneriella* sp.	Chlorophyceae	Chlorophyta	Freshwater	5-15
GMC45	*Diacronema* sp.	Pavlovophyceae	Haptophyta	Marine	10-20
CCAP11/45	*Chlamydomonas reinhardtii*[a]	Chlorophyceae	Chlorophyta	Freshwater	10-30
CCAP979/39	*Cryptomonas pyrenoidifera*	Cryptophyceae	Cryptophyta	Freshwater	15-20
CCAP66/21B	*Tetraselmis chui*	Chlorodendrophyceae	Chlorophyta	Marine	10-15
CCAP981/1	*Cyanophora paradoxa*[a]	Glaucophyceae	Glaucophyta	Freshwater	10-15
CCAP1052/1	*Phaeodactylum tricornutum*[a]	Bacillariophyceae	Bacillariophyta	Marine	15-30
CCAP211/46	*Nannochloropsis* sp.	Eustigmatophyceae	Ochrophyta	Marine	3-5
CCAP19/22	*Dunaliella tertiolecta*	Chlorophyceae	Chlorophyta	Marine	10-15
CCAP927/1	*Isochrysis galbana*	Prymnesiophyceae	Haptophyta	Marine	3-10
CCAP1388/5	*Rhodella violacea*	Rhodellophyceae	Rhodophyta	Marine	10-20

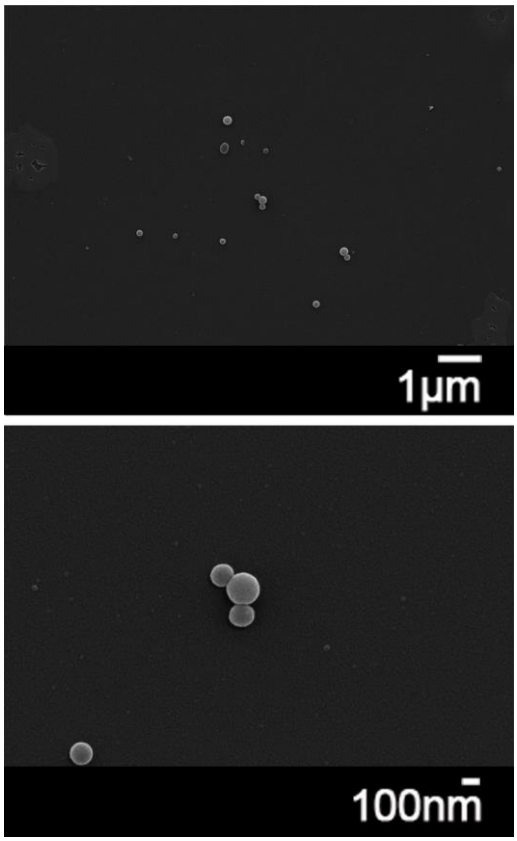
Supplementary File 1. Selected strains from the phytoplankton culture collections at IT Sligo and CCAP. [a] Indicates that the genome of the species has been sequenced.

Strains		*Phaeothamnion sp.*		*Phacodactylum tricormutum*		*Stauroneis sp.*		*Brachyomonas sp.*		*Nannochloropsis sp.*		*Dunaliella tertiolecta*	
Criteria	Weight	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)
'settling' for separation	2	1	2	1	2	1	2	1	2	0	0	0	0
lesser contamination risk	2	2	4	2	4	2	4	2	4	2	4	2	4
sequenced genome	1	0	0	1	1	0	0	0	0	0	0	0	0
[sEV proteins] & n° of particles	2	1	2	1	2	2	4	2	4	1	2	3	6
DLS signal quality	1	0	0	0	0	1	1	1	1	1	1	1	1
size distribution (DLS+NTA)	3	1	3	3	9	2	6	2	6	1	3	2	6
EV Marker 1 (Alix)	1	0	0	2	2	2	2	2	2	2	2	2	2
EV Marker 2 (enolase)	1	0	0	1	1	1	1	1	1	1	1	1	1
EV Marker 3 (others)	1	0	0	0	0	1	1	1	1	1	1	1	1
SEM	2	n.d.	0	2	4	1	2	1	2	n.d.	0	2	4
TOTAL			**11**		**25**		**23**		**23**		**14**		**25**

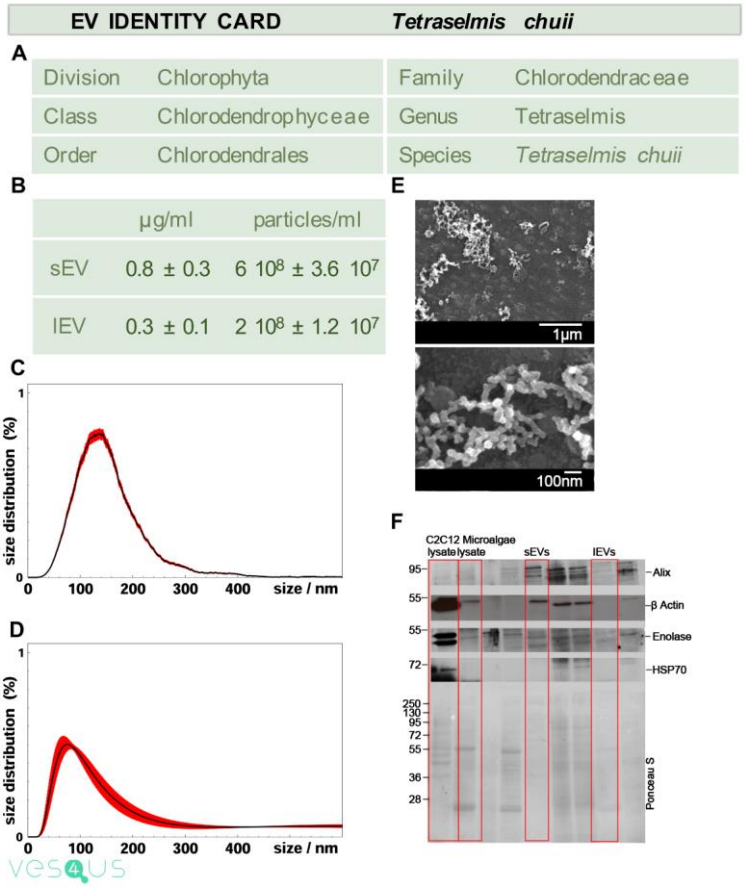
Strains		*Cryptomonas pyrenoidifera*		*Tetraselmis chuii*		*Rhodella violacea*		*Amphidinium sp.*		*Isochrysis galbana*		*Diacronema sp.*	
Criteria	Weight	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)
'settling' for separation	2	1	2	1	2	1	2	1	2	1	2	1	2
lesser contamination risk	2	1	2	2	4	2	4	2	4	2	4	2	4
sequenced genome	1	0	0	0	0	0	0	0	0	0	0	0	0
[sEV proteins] & n° of particles	2	3	6	3	6	2	4	2	4	2	4	2	4
DLS signal quality	1	0	0	1	1	0	0	1	1	1	1	1	1
size distribution (DLS+NTA)	3	1	3	3	9	2	6	3	9	1	3	2	6
EV Marker 1 (Alix)	1	2	2	2	2	2	2	2	2	2	2	0	0
EV Marker 2 (enolase)	1	1	1	1	1	2	2	1	1	1	1	2	2
EV Marker 3 (others)	1	1	1	1	1	1	1	1	1	2	2	0	0
SEM	2	n.d.	0	3	6	3	6	2	4	2	4	3	6
TOTAL			**17**		**28**		**28**		**28**		**23**		**25**

Strains		*Kirchneriella sp.*		*Cyanophora paradoxa*		*Chlamydomonas reinhardtii*		*Unident. Chlorophita*		*Ankistrodesmus sp.*		*Pediastrum sp.*	
Criteria	Weight	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)	Assessm.	Result (AxW)
'settling' for separation	2	0	0	1	2	0	0	1	2	0	0	1	2
lesser contamination risk	2	1	2	1	2	1	2	1	2	1	2	1	2
sequenced genome	1	0	0	1	1	1	1	0	0	0	0	0	0
[sEV proteins] & n° of particles	2	3	6	3	6	3	6	0	0	0	0	1	2
DLS signal quality	1	0	0	1	1	1	1	0	0	0	0	0	0
size distribution (DLS+NTA)	3	2	6	3	9	2	6	2	6	2	6	1	3
EV Marker 1 (Alix)	1	2	2	2	2	0	0	0	0	1	1	2	2
EV Marker 2 (enolase)	1	0	0	1	1	1	1	0	0	1	1	0	0
EV Marker 3 (others)	1	0	0	1	1	0	0	0	0	0	0	0	0
SEM	2	n.d.	0	3	6	3	6	n.d.	0	2	4	n.d.	0
TOTAL			**16**		**31**		**23**		**10**		**14**		**11**

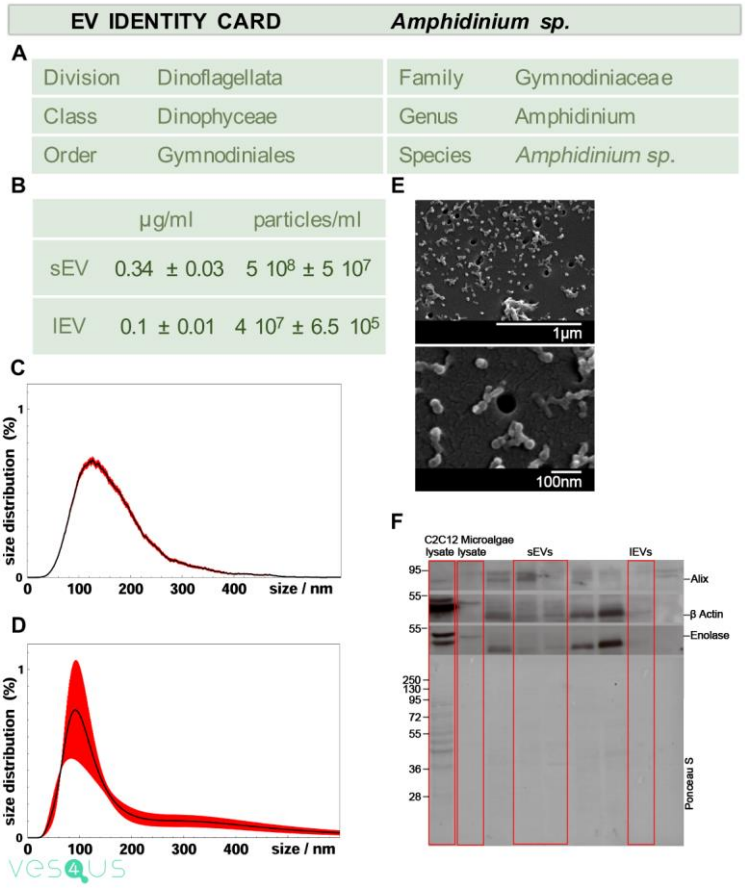
Supplementary File 2. Decision grid for the selection of EV-producing microalgae strains. Legend to the table - W=weight of criterion (1=low; 2=medium; 3=high impact); A=Assessment of option (1=low; 2=medium; 3=high adherence to criteria); Result=AxW.



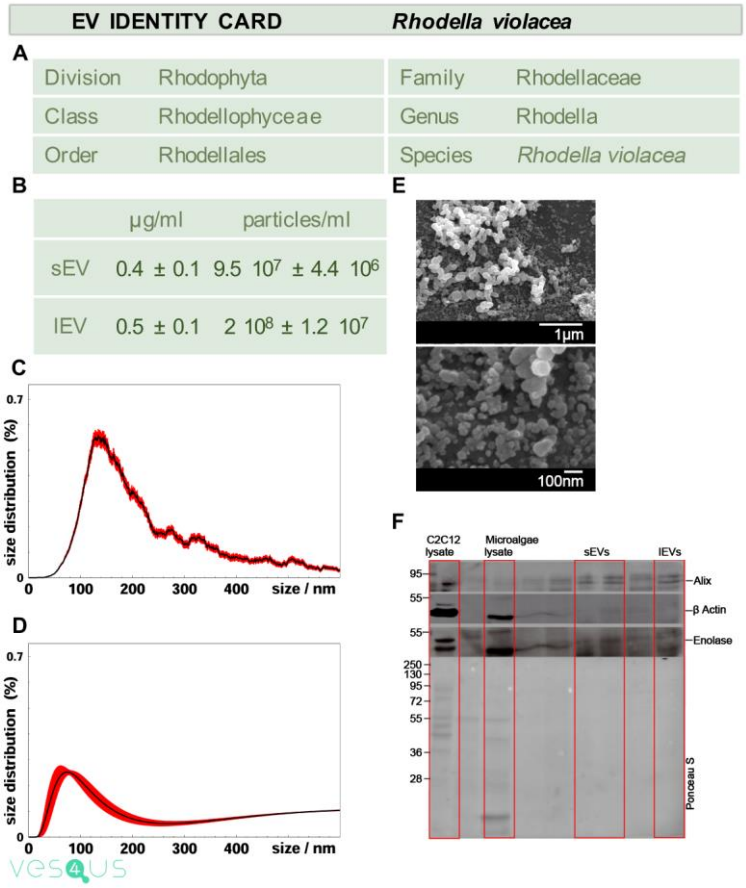
Supplementary File 3. SEM images of a sample process control carried out with PBS instead of microalgal EV preparations showing small amounts of residual spherical osmium nanoprecipitates (as suggested by separate energy dispersive X-ray spectroscopy), which can be caused by aldehyde and alcohol containing reagents.



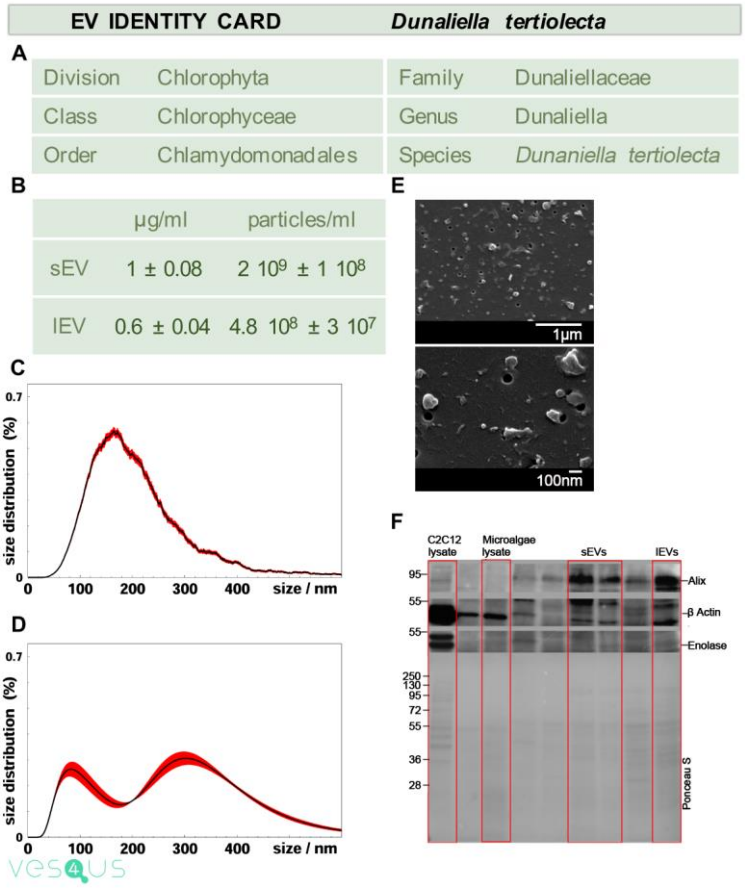
Supplementary File 4. Microalgal EV identity cards: characterisation of extracellular nanoparticles isolated from conditioned media of the indicated microalgal strains. (A) summary scheme on the taxonomy of the microalgal strain; (B) total protein quantification and number of particles of sEV and lEV fractions (data were calculated in triplicate cultures; results are presented by the average value ± standard deviation); (C) nanoparticle tracking analysis (NTA) of sEVs (the distribution error, in red, is calculated using 5 measurements of the same sample); (D) dynamic light scattering (DLS) analysis of sEVs (the distribution error, in red, is calculated using 3 measurements of 3 different samples); (E) representative images of SEM of the sEV fractions; (F) a representative immunoblot of a positive control (lysate of a mammalian cell line, C2C12), microalgal cell lysate, sEV, and lEV fractions.



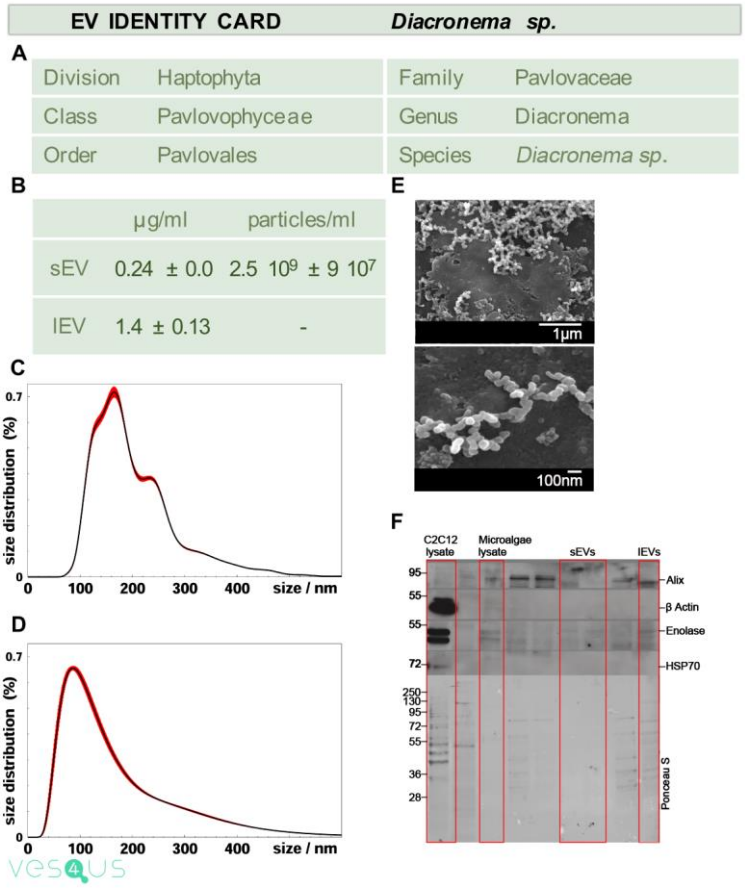
Supplementary File 5. Microalgal EV identity cards: characterisation of extracellular nanoparticles isolated from conditioned media of the indicated microalgal strains. (A) summary scheme on the taxonomy of the microalgal strain; (B) total protein quantification and number of particles of sEV and lEV fractions (data were calculated in triplicate cultures; results are presented by the average value ± standard deviation); (C) nanoparticle tracking analysis (NTA) of sEVs (the distribution error, in red, is calculated using 5 measurements of the same sample); (D) dynamic light scattering (DLS) analysis of sEVs (the distribution error, in red, is calculated using 3 measurements of 3 different samples); (E) representative images of SEM of the sEV fractions; (F) a representative immunoblot of a positive control (lysate of a mammalian cell line, C2C12), microalgal cell lysate, sEV, and lEV fractions.



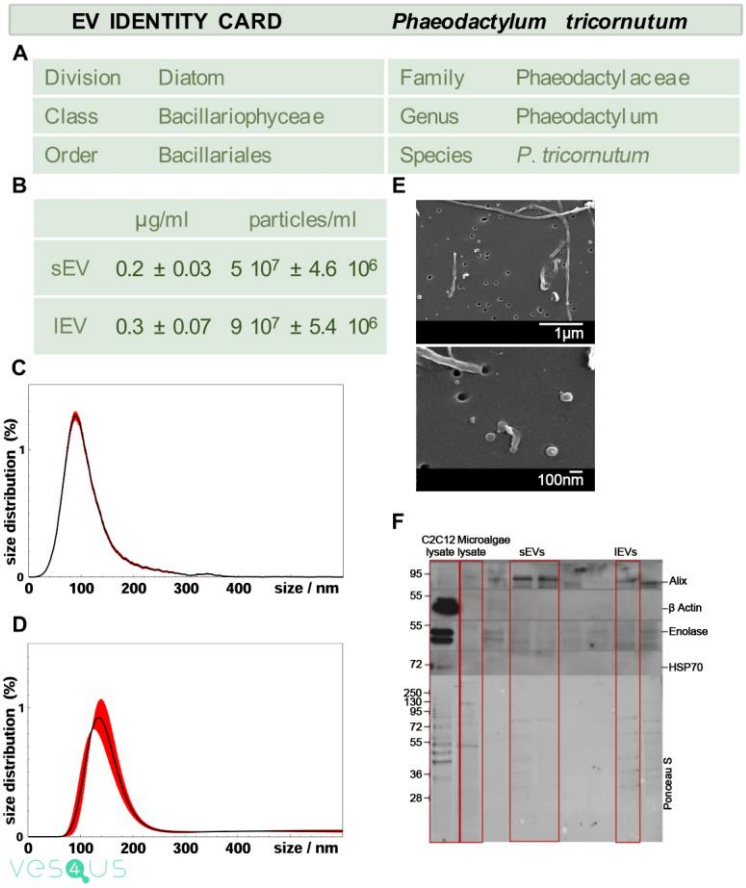
Supplementary File 6. Microalgal EV identity cards: characterisation of extracellular nanoparticles isolated from conditioned media of the indicated microalgal strains. (A) summary scheme on the taxonomy of the microalgal strain; (B) total protein quantification and number of particles of sEV and lEV fractions (data were calculated in triplicate cultures; results are presented by the average value ± standard deviation); (C) nanoparticle tracking analysis (NTA) of sEVs (the distribution error, in red, is calculated using 5 measurements of the same sample); (D) dynamic light scattering (DLS) analysis of sEVs (the distribution error, in red, is calculated using 3 measurements of 3 different samples); (E) representative images of SEM of the sEV fractions; (F) a representative immunoblot of a positive control (lysate of a mammalian cell line, C2C12), microalgal cell lysate, sEV, and lEV fractions.



Supplementary File 7. Microalgal EV identity cards: characterisation of extracellular nanoparticles isolated from conditioned media of the indicated microalgal strains. (A) summary scheme on the taxonomy of the microalgal strain; (B) total protein quantification and number of particles of sEV and lEV fractions (data were calculated in triplicate cultures; results are presented by the average value ± standard deviation); (C) nanoparticle tracking analysis (NTA) of sEVs (the distribution error, in red, is calculated using 5 measurements of the same sample); (D) dynamic light scattering (DLS) analysis of sEVs (the distribution error, in red, is calculated using 3 measurements of 3 different samples); (E) representative images of SEM of the sEV fractions; (F) a representative immunoblot of a positive control (lysate of a mammalian cell line, C2C12), microalgal cell lysate, sEV, and lEV fractions.

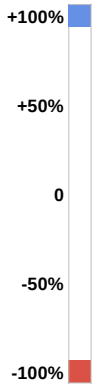


Supplementary File 8. Microalgal EV identity cards: characterisation of extracellular nanoparticles isolated from conditioned media of the indicated microalgal strains. (A) summary scheme on the taxonomy of the microalgal strain; (B) total protein quantification and number of particles of sEV and lEV fractions (data were calculated in triplicate cultures; results are presented by the average value ± standard deviation); (C) nanoparticle tracking analysis (NTA) of sEVs (the distribution error, in red, is calculated using 5 measurements of the same sample); (D) dynamic light scattering (DLS) analysis of sEVs (the distribution error, in red, is calculated using 3 measurements of 3 different samples); (E) representative images of SEM of the sEV fractions; (F) a representative immunoblot of a positive control (lysate of a mammalian cell line, C2C12), microalgal cell lysate, sEV, and lEV fractions.



Supplementary File 9. Microalgal EV identity cards: characterisation of extracellular nanoparticles isolated from conditioned media of the indicated microalgal strains. (A) summary scheme on the taxonomy of the microalgal strain; (B) total protein quantification and number of particles of sEV and lEV fractions (data were calculated in triplicate cultures; results are presented by the average value ± standard deviation); (C) nanoparticle tracking analysis (NTA) of sEVs (the distribution error, in red, is calculated using 5 measurements of the same sample); (D) dynamic light scattering (DLS) analysis of sEVs (the distribution error, in red, is calculated using 3 measurements of 3 different samples); (E) representative images of SEM of the sEV fractions; (F) a representative immunoblot of a positive control (lysate of a mammalian cell line, C2C12), microalgal cell lysate, sEV, and lEV fractions.

βActin	-12					
Enolase	-22	-11				
Alix	-36	-02	+02			
DLS signal & particle N.	+47	+20	+24	-37		
Average Size	-18	-17	-33	+41	-51	
Size Range (PDI)	-25	-21	-03	-31	-38	-40
Properties	BCA	βActin	Enolase	Alix	DLS signal & Particle N.	Average Size



Supplementary File 10. Correlation matrix for the selection of EV-producing microalgae strains over the following variables: (1) EVs protein content with respect to culture medium in terms of BCA assay, (2)-(4) the amount of EV markers for enolase, Alix, b-Actin in terms of band densitometry, (5) the total scattering signal for sEV sample (with equal protein concentration), (6) the average size, (7) the size range, in terms of Polydispersity Index, PDI (measured as the ratio of the variance and the square average of the size distribution). Given the vector X_i (i=1,..7) including the N=18 values for each of the 7 variables considered, one may derive a centered and normalised vector $Z_i = [X_i - \text{mean}(X_i)]/\text{variance}(X_i)/\text{sqrt}(N-1)$, and the (18x7) data matrix Z, whose columns are the vectors Z_i. Given Z' as the transpost of Z, the correlation matrix is defined as the product Z'Z. In the table, the values are reported in terms of percentage.