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APPENDICES

APPENDIX A
REAGENTS AND MEDIAS

REAGENTS AND MEDIAS

Reagents for DNA cloning into plasmid vector

1. Luria-Bertani medium (LB) per litre

   - LB media 15 g
   - Add deionized H_2O to 1 litre and autoclave for 20 min at 15 lb/sq

2. LB agar per litre

   - LB media 15 g
   - Nutrient agar 15 g
   - Add deionized to 1 litre and autoclave for 20 min at 15 lb/sq

3. SOC media per litre

   - LB media 15 g
   - NaCl 0.05 g
   - Add deionized autoclaved H_2O to remove 950 ml. Then add 10 ml of 250 mM KCl solution. Adjust the pH to 7.0 and then add more deionized autoclaved H_2O to 975 ml. Solution was steriled by autoclave for 20 min at 15 lb/sq. Just before use, add 5 ml of sterile 2 M $MgCl_2$ and 20 ml of sterile 1 M solution glucose.

Reagents for agarose gel electrophoresis

1. 0.8% agarose gel

   - Agarose 0.8 g
   - 1X TAE buffer 100 ml
   - Dissolved by microwave for 1 min

2. 50X TAE buffer per litre

   - Tris base 242 g
   - Acetic acid 57.1 ml
   - 0.5 M EDTA, pH 8.0 100 ml

3. Ethidium bromide (10 mg/ml)

   - Ethidium bromide 10 mg
   - Distilled water to 1 ml

4. 6X gel loading dye

- 0.25% bromophenol blue
- 0.25% xylene cyanol FF
- 30% glycerol

Reagents for polymerase chain reaction

1. PCR reaction mixture or Master mix (500 µl)

- 25 mM MgCl	36	µl
- 10X PCR buffer	60	µl
- 10 mM dNTPs	6	µl
- 5 U/µl Taq polymerase	3	µl

- Add deionized autoclaved H_2O to volumn 500 µl

2. dNTPs 10 mM (mixture)

- 10 mM dATP	20 µl of 100 mM
- 10 mM dTTP	20 µl of 100 mM
- 10 mM dCTP	20 µl of 100 mM
- 10 mM dGTP	20 µl of 100 mM

- Add deionized autoclaved water 120 µl

Stock Solutions for protein expression in *P. pastoris*

1. 10X YNB

- yeast nitrogen base (YNB) with ammonium sulfate and without amino acids 134 g

- Dissolve in 1000 ml of water and filter sterilize. Heat the solution to dissolve YNB completely in water. Store at +4°C.

- Alternatively, use 34 g of YNB without ammonium sulfate and amino acids and 100 g of ammonium sulfate.

2. 500X B (0.02% Biotin)

- Biotin 20 mg
- Dissolve in 100 ml of water and filter sterilize. Store at +4°C.

3. 10X D (20% Dextrose)

- D-glucose 200 g

- Dissolve of in 1000 ml of water. Autoclave for 15 minutes or filter sterilize.

4. 10X M (5% Methanol)

- Mix 5 ml of methanol with 95 ml of water. Filter sterilize and store at +4°C. The shelf life of this solution is approximately two months.

5. 10X GY (10% Glycerol)

- Glycerol 100 ml

- Mix with 900 ml of water. Sterilize either by filtering or autoclaving. Store at room temperature. The shelf life of this solution is greater than one year.

6. 1 M potassium phosphate buffer, pH 6.0

- 1 M K_2HPO_4 132 ml

- 1 M KH2PO4 868 ml

- Confirm the pH = 6.0 ± 0.1 (if the pH needs to be adjusted, use phosphoric acid or KOH). Sterilize by autoclaving and store at room temperature.

Reagents and medias for protein expression in *P. pastoris*

1. Low Salt LB Medium with Zeocin™

- Tryptone 10 g
- NaCl 5 g
- Yeast extract 5 g

- Add distilled H_2O to 950 ml. Adjust pH to 7.5 with 1N NaOH. Bring the volume up to 1 liter. For plates, add 15 g/L agar before autoclaving.

- Autoclave on liquid cycle at 15 psi and 121°C for 20 minutes.

- Allow the medium to cool to at least 55°C before adding the Zeocin™ to 25 µg/ml final concentration.

- Store plates at +4°C in the dark. Plates containing Zeocin™ are stable for up to 2 weeks.

2. Yeast Extract Peptone Dextrose Medium (YPD) (1 liter)

- Yeast extract 10 g
- Peptone 20 g

- Dissolve in 900 ml of water.
- Include 20 g of agar if making YPD slants or plates.
- Autoclave for 20 minutes on liquid cycle.
- Add 100 ml of 20% dextrose (filter-sterilize dextrose before use).
- Cool solution to ~60°C and add the appropriate amount of Zeocinô from a 100 mg/ml stock solution. Note: It is necessary to include Zeocin™ in the medium for selection of *Pichia* transformants only. Zeocin™ may be omitted from the medium when performing expression studies.
- Store YPD slants or plates containing Zeocin™ at +4°C. The shelf life is one to two weeks.

3. Yeast Extract Peptone Dextrose Medium with Sorbitol (YPDS) (1 liter)

- Yeast extract 10 g
- Sorbitol 182.2 g
- Peptone 20 g

- Dissolve in 900 ml of water. Add 20 g of agar. Autoclave for 20 minutes on liquid cycle. Add 100 ml of 20% dextrose (filter-sterilize dextrose before use). Cool solution to ~60°C and add the appropriate amount of Zeocin™ from a 100 mg/ml stock solution. Note: It is necessary to include Zeocin™ in the medium for selection of *Pichia* transformants only. Zeocin™ may be omitted from the medium Zeocin™ when performing expression studies. Store YPDS slants or plates containing Zeocin™ at +4°C. The shelf life is one to two weeks.

4. Buffered Glycerol-complex Medium (BMMY) (1 liter)
Buffered Methanol-complex Medium (BMGY) (1 liter)

- Yeast extract 10 g,
- Peptone 20 g

- Dissolve in 700 ml water. Autoclave 20 minutes on liquid cycle. Cool to room temperature, then add the following and mix well:
- Add 100 ml 1 M potassium phosphate buffer, pH 6.0
100 ml 10X YNB
2 ml 500X B
100 ml 10X GY
- For BMMY, add 100 ml 10X M instead of glycerol.

- Store media at +4°C. The shelf life of this solution is approximately two months.

Color development solution

1. DAB substrate solution (25 mg/ml)

- Diaminobenzidine (DAB)	1	g
- Distrilled water	40	ml

-Aliquots in 1 ml and kept at -20 °C

2 Tris-base buffer (pH 7.6)

-Tris	6.1	g
-distilled H_2O	1	L

- Add DAB substrate solution 1 ml into Tris-base buffer 50 ml, then add H_2O_2 50 µl. The DAB substrate solution mixture should prepared 5-10 min before used.

Buffers for protein purification

1. 1 M Phosphate buffer

- $NaH_2PO_4.H_2O$	5.2	g
- Na_2HPO_4	23.0	g
-distilled H_2O	200	ml

2. Binding buffer/Wash buffer 1 litre (pH 7.4)

- 1 M Phosphate buffer	20	ml
- NaCl	29.22	g
- Imidazole	1.36	g
- Urea	480.48	g

3. Elution buffer 1 litre (pH 7.4)

- 1 M Phosphate buffer	20	ml
- NaCl	29.22	g
- Imidazole	34.04	g
- Urea	480.48	g

Buffers for protein manipulation

1. 15 % separating gel

- 1.5 M Tris-HCl pH 8.8	2.5	ml
- 30 % Acrylamide/Bis	5	ml
- 10 % SDS	100	µl
- TEMED	2.5	µl
- Distilled H_2O	5	ml
-10 % ammonium persulphat	100	µl

2. 5% Stacking gel

- 1 M Tris-base pH 6.8	312.5	µl
- 30 % Acrylamide/Bis	312.5	µl
- 10 % SDS	25	µl
- TEMED	10	µl
- Distilled H_2O	1.813	ml
-10 % ammonium persulphate	50	µl

3. SDS-PAGE sample buffer

- Distilled H_2O	3.8	ml
- 0.5 M Tris-HCl, pH 6.8	1	ml
- Glycerol	0.8	ml
- 10 % (w/v) SDS	1.6	ml
- 2-mercaptoethanol	0.4	ml
- 1 % (w/v) bromophenol blue	0.4	ml

Store at room temperature

4. 5x running buffer

- Tris	9	g
-Glycine	43.2	g
- SDS	3	g

Add milliQ water to 600 ml and store at 4°C

5. 1x Transfer buffer
   - 10 % methanol
   - 0.5x running buffer

APPENDIX B
SEQUENCES

SEQUENCES

***Opisthorchis viverrini* cathepsin B2 mRNA, complete cds**

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VERSION     GQ303560.1  GI:255040224
KEYWORDS    .
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REFERENCE   1 (bases 1 to 1014)
AUTHORS     Sripa,J., Laha,T., To,J., Brindley,P.J., Sripa,B., Kaewkes,S.,
            Dalton,J.P. and Robinson,M.W.
TITLE       Secreted cysteine proteases of the carcinogenic liver fluke,
            Opisthorchis viverrini: regulation of cathepsin F activation by
autocatalysis and trans-processing by cathepsin B
JOURNAL     Cell. Microbiol. (2010) In press
PUBMED      20070308
REMARK      Publication Status: Available-Online prior to print
REFERENCE   2 (bases 1 to 1014)
AUTHORS     Sripa,J., Laha,T., To,J., Xu,W., Dalton,J.P., Brindley,P.J.,
            Loukas,A. and Robinson,M.W.
TITLE       Direct Submission
JOURNAL     Submitted (22-JUN-2009) Department of Parasitology, Faculty of Medicine,
Khon Kaen University, Mittaparp Road, Khon Kaen 40002, Thailand
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***Opisthorchis viverrini* truncated cathepsin B mRNA, complete cds**

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REFERENCE   1  (bases 1 to 942)
AUTHORS     Sripa,J., Laha,T., To,J., Brindley,P.J., Sripa,B., Kaewkes,S.,
            Dalton,J.P. and Robinson,M.W.
TITLE       Secreted cysteine proteases of the carcinogenic liver fluke,
            Opisthorchis viverrini: regulation of cathepsin F activation by
            autocatalysis and trans-processing by cathepsin B
JOURNAL     Cell. Microbiol. (2010) In press
PUBMED      20070308
REMARK      Publication Status: Available-Online prior to print
REFERENCE   2  (bases 1 to 942)
AUTHORS     Sripa,J., Laha,T., To,J., Xu,W., Dalton,J.P., Brindley,P.J.,
            Loukas,A. and Robinson,M.W.
TITLE       Direct Submission
JOURNAL     Submitted (22-JUN-2009) Department of Parasitology, Faculty of
            Medicine, Khon Kaen University, Mittaparp Road, Khon Kaen 40002,
            Thailand
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APPENDIX C
SUPPLEMENTARY

SUPPLEMENTARY

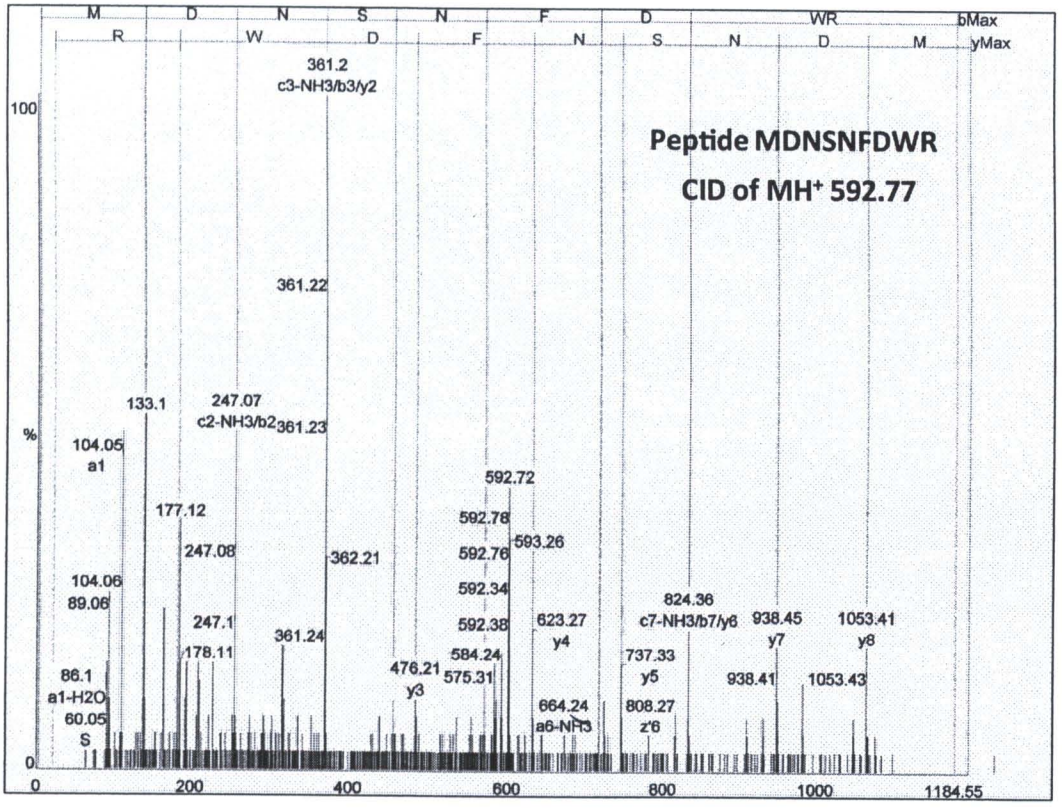

Figure S1 MS/MS data for *Ov*-CF-1 N-terminal peptide following *trans* activation by *Ov*-CB-1.

APPENDIX D

RESEARCH PUBLICATIONS

RESEARCH PUBLICATIONS

1. **Sripa J.**, Laha T., To J., Brindley P. J., Sripa B., Kaewkes S., et al. (2010). Secreted cysteine proteases of the carcinogenic liver fluke, *Opisthorchis viverrini*: regulation of cathepsin F activation by autocatalysis and trans-processing by cathepsin B. **Cell Microbiol**, 12(6), 781-95.

2. **Sripa J.**, Pinlaor P., Brindley PJ., Sripa B., Kaewkes S., Robinson MW., et al. (2011). RNA interference targeting cathepsin B of the carcinogenic liver fluke, *Opisthorchis viverrini.* **Parasitol Int**. (in press)

3. **Sripa J.**, Brindley PJ., Sripa B., Loukas A., Kaewkes S., Laha T. (2011). Evaluation of the liver fluke cathepsin B protease, *Ov*-CB-1, as a serodiagnostic antigen for human opisthorchiasis. **Parasitol Int**. (accepted)

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Scholarship received:

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