



Prostate Cancer Symposium

October 2, 2010 • New York University Kimmel Center for University Life • New York, NY

Prostate Net Health Scholar Poster Winners Presentations

Mark Litwin, MD

Introduction of Winners



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Jacquelyne Gaddy MS

Brittany Jones



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Brittany Jones

**Therapeutic Potential of Curcumin:
Inhibition of MIC-1/GDF-15 Expression
in Prostate Cancer Cells Exposed to
Heavy Metal Carcinogen**

By: Brittany Jones

Macrophage inhibitory cytokine 1(MIC-1)

MIC-1 – Member of human Transforming Growth Factor β (TGF β).

- Not expressed under basal conditions except in placenta and prostate tissue but induced by inflammation, injury or malignancy.
- First isolated from a monocytoid cell line U937 placenta and spleen by subtraction cDNA library enriched for genes associated with macrophage activation.
- a disulphide –linked dimer of 30 kDa and monomer of 15 kDa.
- Large increase in serum MIC-1 from normal serum levels of 250-1250 pg/ml, to 100,000pg/ml in prostate cancer.
- MIC -1 expression is upregulated in response to oxygen deprivation condition in glioblastoma cell lines.

Nickel chloride (NiCl₂) and Cobalt Chloride (CoCl₂)

- Heavy metals like Nickel and Cobalt are major environmental pollutants and is hazardous to human health.
- ➔ Workers exposed to Ni and Co compounds has been shown to correlate with the development of nasal, lung
- and prostate cancer etc.
- ➔ NiCl₂ and CoCl₂ treatment *in vitro* mimic hypoxic and anoxic conditions.

Curcumin (C₂₁H₂₀O₅)

Curcumin, a component of turmeric, is derived from the roots (rhizomes) of the plant *Curcuma longa*.

- ➡
- ➡ Used in traditional Ayurvedic medicine in India and other Asian countries for at least 6000 years.
- ➡ Chemically known as diferuloylmethane (C₂₁H₂₀O₆)
- ➡ Has anti-inflammatory, anti-oxidant, anti-toxic, anti-tumor, and potentially chemotherapeutic properties.



HEAVY METALS
(NiCl₂, CoCl₂)
(Oxidative Stress)

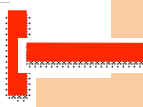


HYPOXIA



NFκB

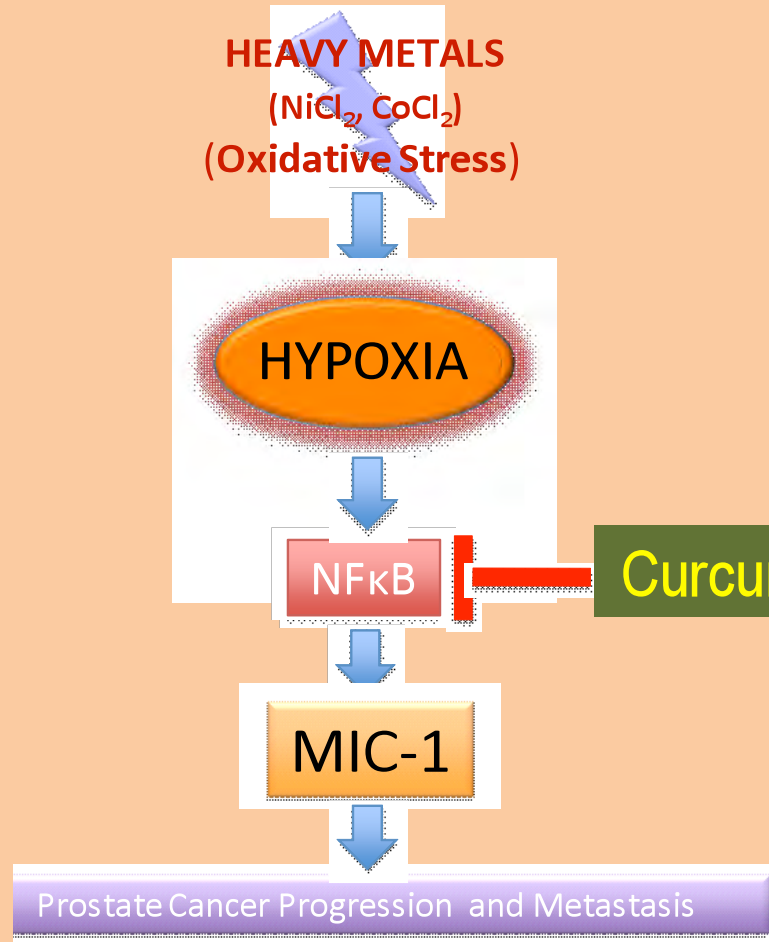
Curcumin



MIC-1



Prostate Cancer Progression and Metastasis



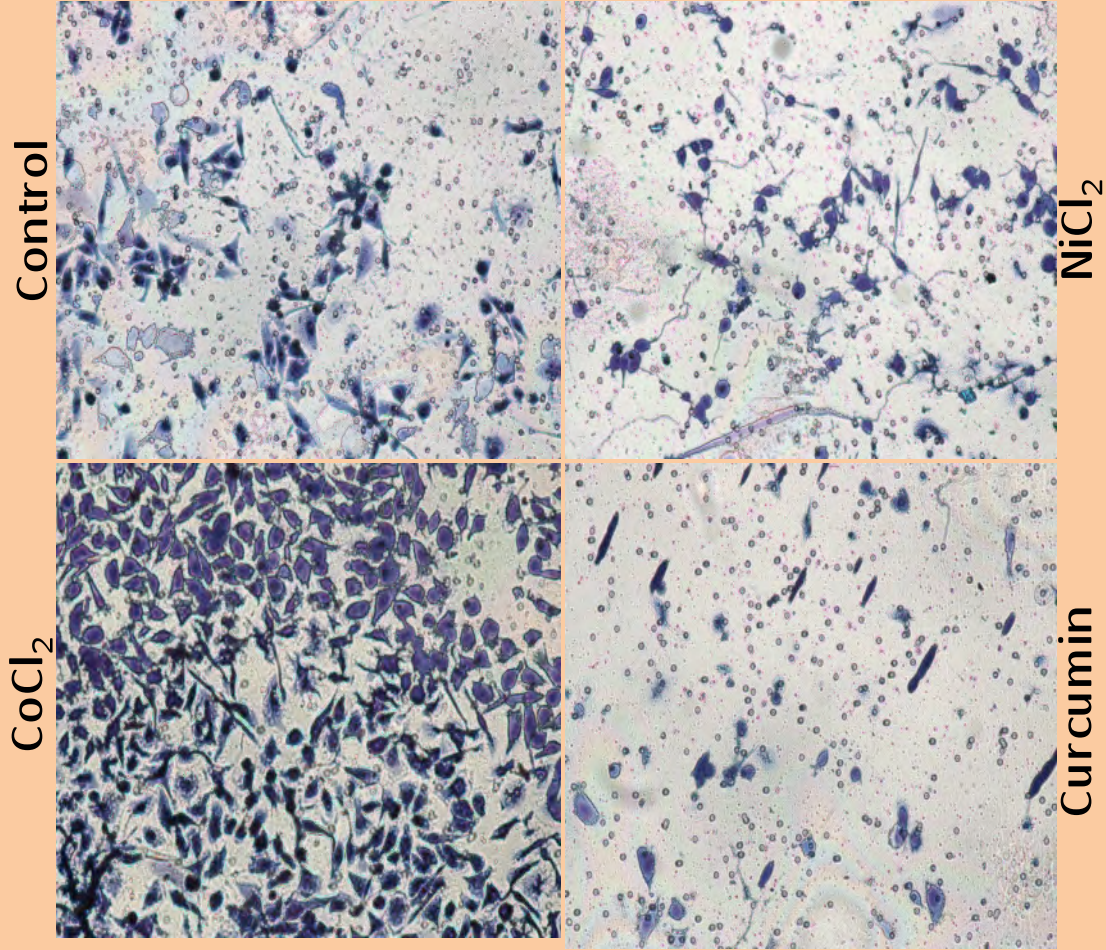
Hypothesis

- Therapeutic potential of Curcumin inhibiting MIC-1 expression in response to heavy metal induced hypoxic condition.

Methodology

- ➔ Treatment of NiCl₂ (1 mM), CoCl₂ (400μM) in prostate cancer cell lines to mimic hypoxic condition.
- ➔ MIC-1/GDF-15 mRNA expression was analyzed by RT-PCR and Quantitative Real-Time PCR.
- ➔ Secreted MIC-1/GDF-15 was analyzed by Western blot using α-MIC-1 antibody (1:500) in the concentrated supernatant of cultured cells.
- ➔ Effect of Curcumin on MIC-1/GDF-15 expression was studied at mRNA level by RT-PCR and Quantitative Real-Time PCR.
- ➔ Effect of NiCl₂, CoCl₂ and Curcumin on cellular motility of prostate cancer cells was studied by Boyden's chamber motility assay.

Results- Motility Assay



Conclusion

- Overall, our data demonstrate the tumor suppressive effect of Curcumin by down regulating MIC-1 expression induced in response to heavy metal (NiCl_2 , CoCl_2) mediated hypoxic condition in prostate cancer cells.

Future Direction

- ➔ The potential tumor suppressive function of Curcumin will be validated in multiple prostate cancer cells *in vitro*
 - as well as *in vivo* in prostate orthotopic mouse models.
- ➔ Mechanism of both NiCl₂ and CoCl₂ mediated overexpression and Curcumin mediated down regulation of
 - MIC-1 will be investigated. ,



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