Conclusions

The conclusions derived from the experimental work presented are the following ones:

1. IFN-γ makes macrophages unresponsive to apoptotic stimuli by both, induction of $p21^{Waf1}$ expression and blockade of the cell cycle at the G_1/S boundary.

2. Decorin inhibits M-CSF-dependent proliferation of macrophages in a process that requires expression of $p27^{Kip1}$.

3. Decorin protects macrophages against apoptosis induced by growth factors starvation through a mechanism that is dependent on $p21^{Waf1}$ expression.

4. Decorin enhances the IFN-γ and LPS induced activation of macrophages. This effect depends on the ability of decorin to block the binding of autocrine-produced TGF-β on the surface of macrophages.

5. Using phage display we have isolated a β5 binding peptide that mimics annexin V. This peptide has been used to identify annexin as a β5 cytoplasmic domain-binding molecule.

6. Internalization of the β5-binding peptide induces apoptosis in endothelial cells by regulation of the annexin V-dependent PKC activity.

7. We have identified XIAP binding peptides that modulate cell viability and apoptosis

8. We have developed a new technology for the characterization of cell surface molecules using phage-displayed peptide libraries. This method has been used to isolate a peptide that mimics the binding site of $VEGF_{165}$ to the VEGF receptor and NRP-1

9. Phage display is a suitable technique for the characterization of the diversity of cell surface molecules in the human vasculature with high possibilities for developing therapeutic strategies. As proof of principle, a potential mimetope of interleukin-11 (IL-11) has been isolated from prostate and shown to be tissue specific.

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Appendix

Marina Cardó Vila has published the following articles as Ph.D. student

PUBLICATIONS

1.- Xaus J, **Cardó M**, Valledor AF, Soler C, Lloberas J, Celada A. Interferon gamma induces the expression of p21waf-1 and arrests macrophage cell cycle, preventing induction of apoptosis. Immunity. 1999 Jul;11(1):103-13.

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BOOK CHAPTERS

- Syrigos KN and Harrington KJ. 2003.Targeted therapy for cancer. Published in the United States by Oxford University Press Inc., New York. Chapter 14: *Targeting blood vessels in vivo by using phage display libraries*. Vidal C., **Cardó-Vila M.,** Lahdenranta J., Arap W. and Pasqualini R. pp 250-255.