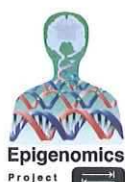


# Modélisation de systèmes biologiques complexes dans le contexte de la génomique



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FOURMENTIN-GUILBERT



# Computer simulation of Multiple Myeloma in the context of Systems Biology

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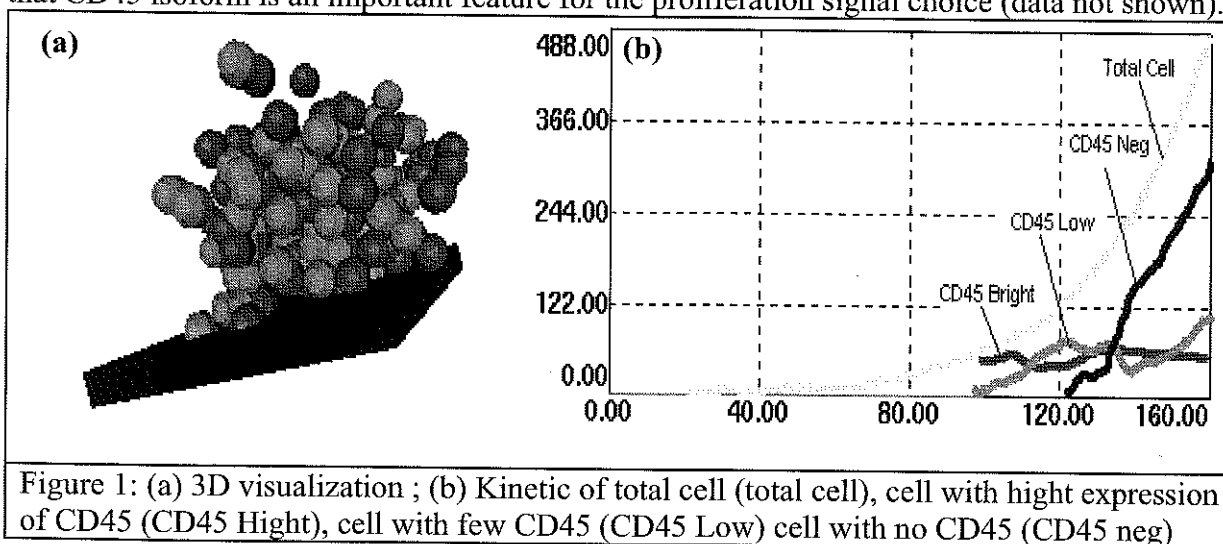
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Cancer is complex adaptive system. We assume that multiple myeloma (MM) can be study in the context of complexity using Systems Biology (SB). SB is a new field in biology aims at understanding biology at systems level. We develop the "In Virtuo" experimentation for SB using virtual environment. Multiagent systems provide an attractive computer framework for SB and "In Virtuo" approaches.

We implement a computer simulation supporting the maturation model of myeloma cells based on the CD45 expression. One has shown that CD45 expression decreases with the maturation of the cells and CD45 annihilation is a critical pronostic for patient survival. CD45 expression is also necessary for IL6 proliferation signal but inhibits IGF-1 proliferation signal. Moreover, CD45 expression is stimulate by IL6 and its activity inhibited by dimerization . The kinetic of CD45 dimerization depends of the molecule isoform.

So, we have developed a computer simulation based on a multiagent system which integrates the model of myeloma cell previously described in their micro-environnement.

The simulation shows that kinetic of MM tumor presents an exponential shape (Figure 1) which is characteristic of the first stages of tumor growth. Next, we can observe the lost of tumor connectivity, which was previously shown to occur with tumor evolution. We assume that CD45 isoform is an important feature for the proliferation signal choice (data not shown).



Holistic study, by the way of "In Virtuo" simulation enables to simulate emergent behaviour of MM. The simulation shows the importance of the microenvironnement and the CD45 isoform for tumor evolution. Moreover, we assume that our original approach may allows research of new therapeutical targets and therapies.