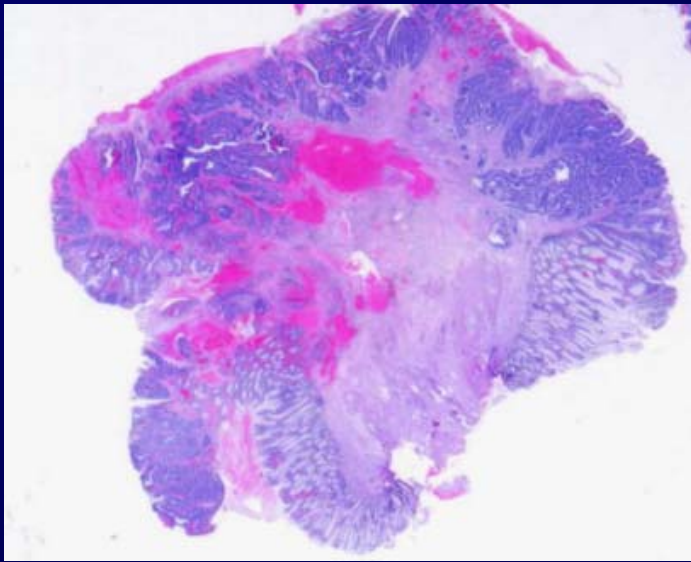


# **MOLECULAR PROFILING OF FOBT-DETECTED COLORECTAL POLYPS**

**Risio M, Senore C, Pera A, Segnan N.**



## **Polipi FOBT+** *Il Polipo “Sanguinante”*

- **E' identificato casualmente (“*Random Detection*”) dal Test FOBT tra i Polipi Adenomatosi, prevalentemente di Tipo avanzato.**

**OPPURE**

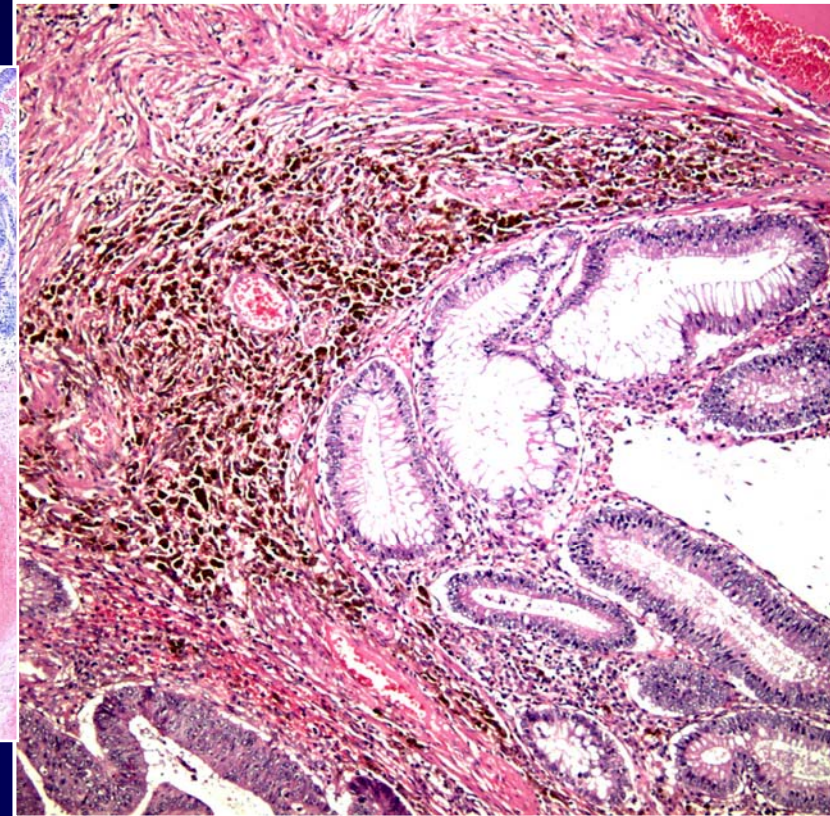
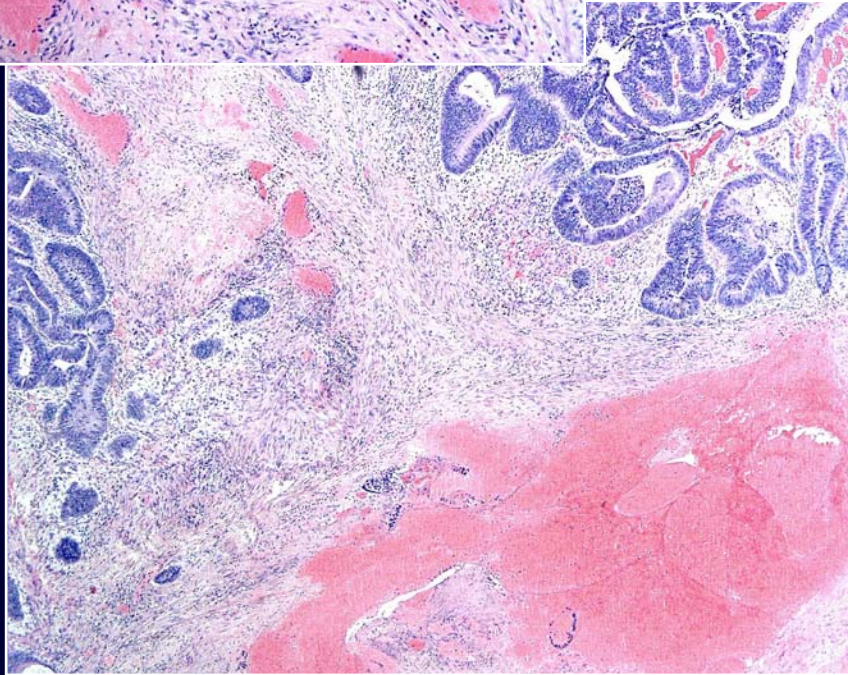
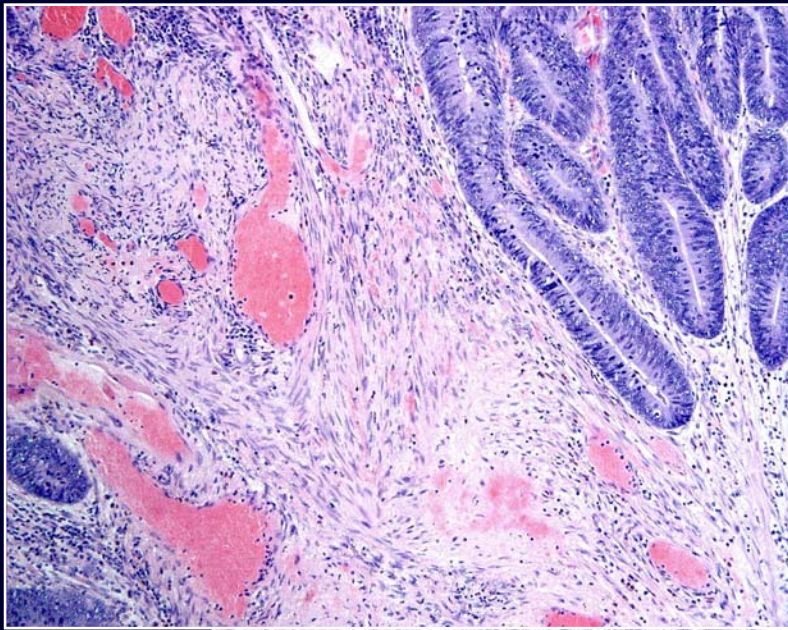
- **E' un sottogruppo di Polipi Adenomatosi Avanzati, con Meiotragia al Sanguinamento, il cui Fenotipo è espressione di un percorso genetico-molecolare differenziato.**



**Storia Naturale Diversificata ?**

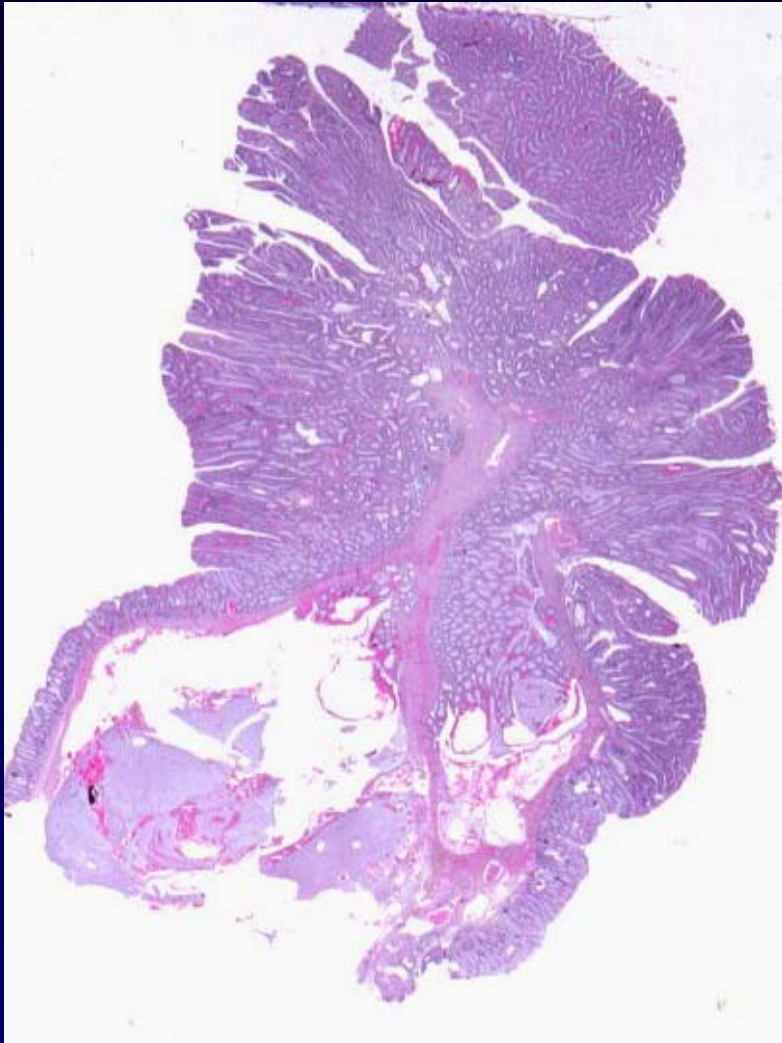


**Il Sanguinamento Profondo  
e la  
Distopia Sottomucosa  
(c.d. “PseudoInvasione”)**





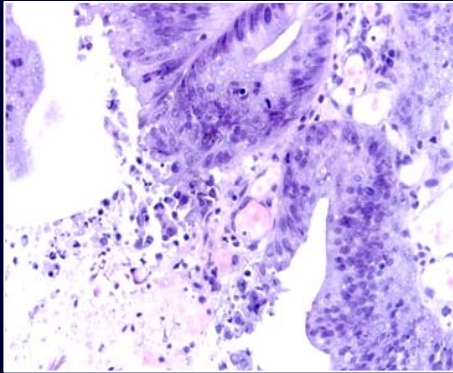
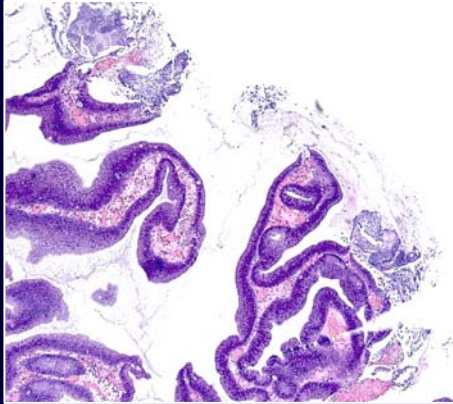
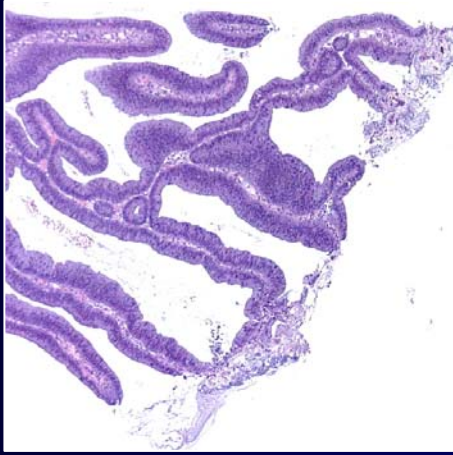
# Il Sanguinamento Profondo e la Distopia Sottomucosa (c.d. “PseudoInvasione”)



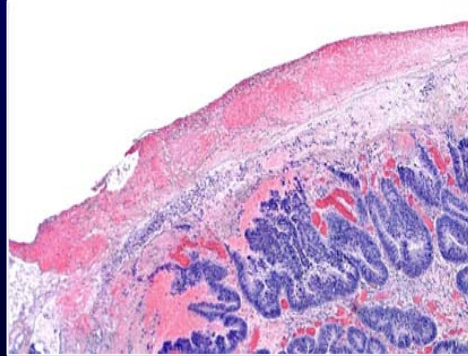
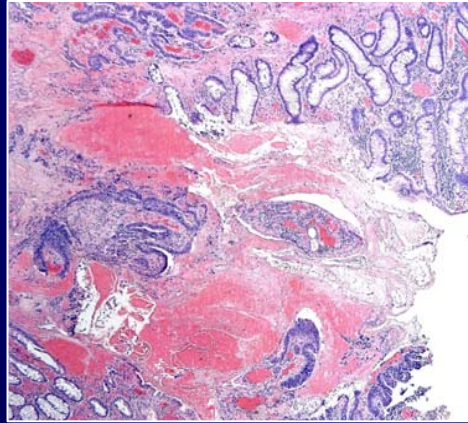
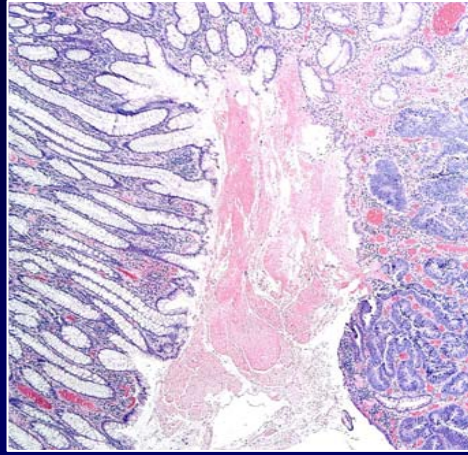
*“...A seguito di ripetute torsioni cui vanno prevalentemente ma non esclusivamente i polipi con lungo peduncolo può verificarsi la erniazione in sede sottomucosa.....”*

# Morfogenesi del Sanguinamento Endoluminale

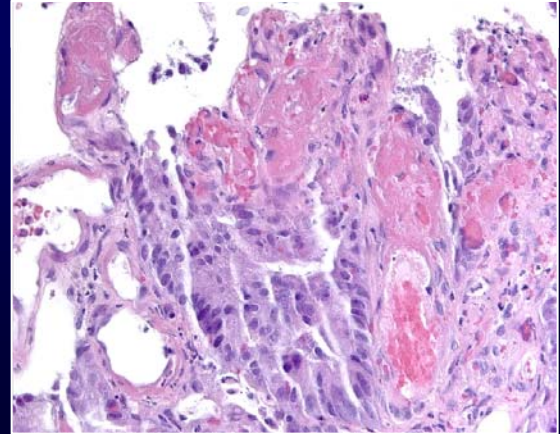
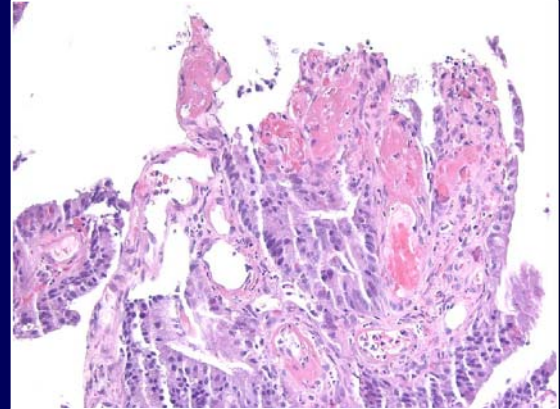
F  
A  
S  
E  
1



F  
A  
S  
E  
2



F  
A  
S  
E  
3



# Istologia del Sanguinamento Endoluminale: Distribuzione per Modalità di Detezione

	Negativi	Fase 1	Fase 2	Fase 3	Totale
<b>FOBT</b>	<b>7 / 33</b>	<b>8 / 33</b>	<b>12 / 33</b>	<b>6 / 33</b>	<b>26 / 33 (79%)</b>
<b>Endoscopia</b>	<b>84 / 90</b>	<b>10 / 90</b>	<b>4 / 90</b>	<b>2 / 90</b>	<b>16 / 90 (18%)</b>

**p = 0.0001**

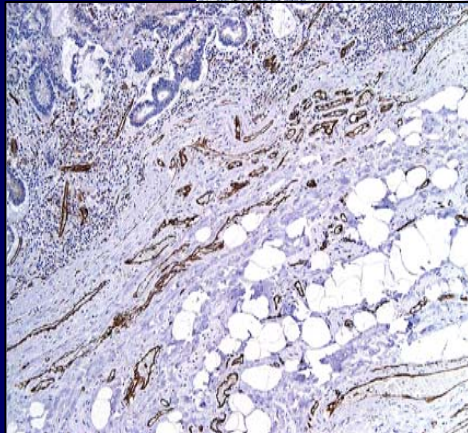
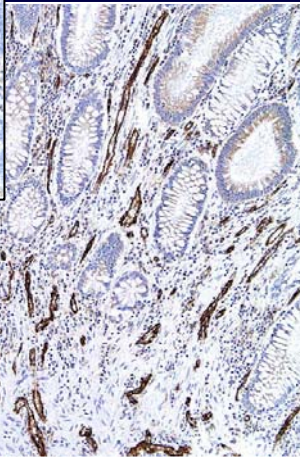
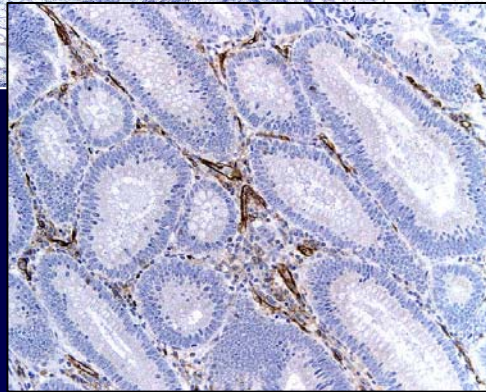
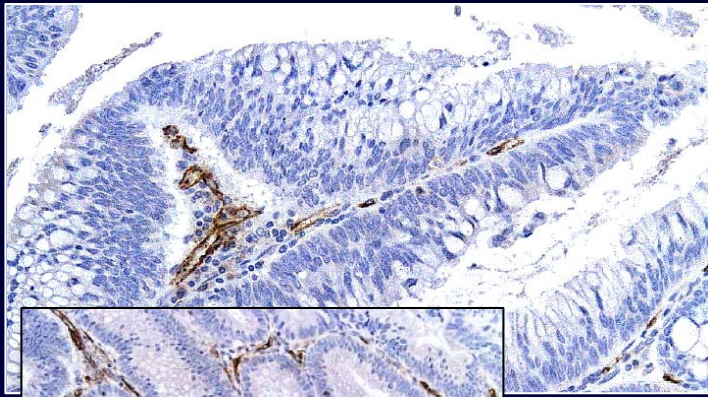
# Polipi FOBT+:

## Caratteristiche Clinico-Patologiche

	<b>Polipi Iperplastici</b>	<b>Adenoma T LG &lt;1cm</b>	<b>Adenoma TV/HG &lt;1cm</b>	<b>Adenoma T LG &gt;1cm</b>	<b>Adenoma TV/HG &gt;1cm</b>
<b>Polipo Peduncolato FOBT</b>	<b>2 (5%)</b>	<b>10 (14%)</b>	<b>7 (33%)</b>	<b>42 (69%)</b>	<b>59 (64%)</b>
<b>Polipo Peduncolato Endoscopia</b>	<b>18 (5%)</b>	<b>62 (14%)</b>	<b>21 (28%)</b>	<b>91 (66%)</b>	<b>96 (75%)</b>



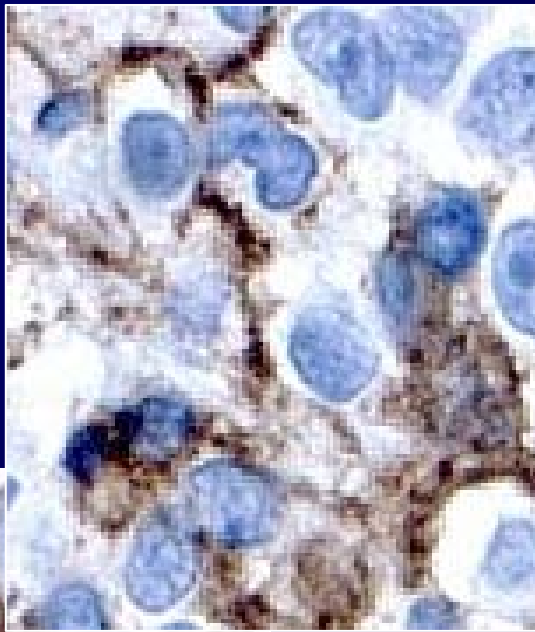
# Polipi FOBT+: L'Impalcatura Microvascolare



**DENSITÀ MICROVASCOLARE  
(MVD)**  
Numero di Microvasi CD31+ / mm<sup>2</sup>

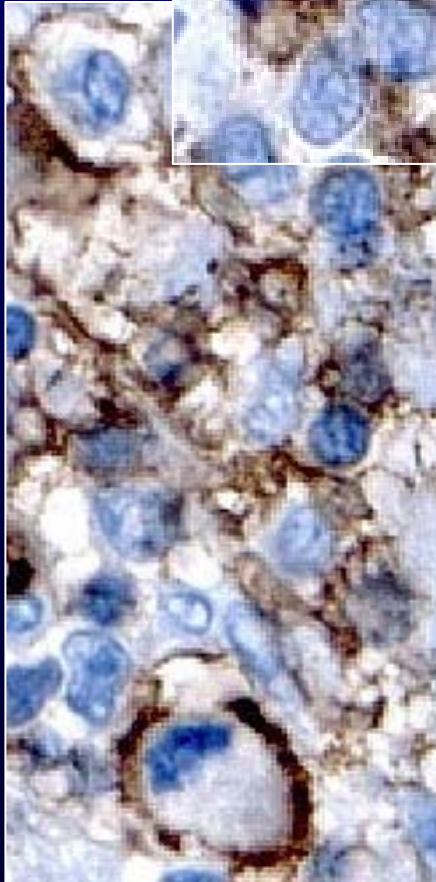
	Asse dei Villi	Aree Tubulari (1/2 Profonda)	Aree Tubulari (1/2 Superficiale)	Sottomucosa
<b>POLIP FOBT</b>	<b>3,5</b>	<b>8,6</b>	<b>5,9</b>	<b>4,2</b>
<b>POLIP ENDOSCOPIA</b>	<b>4,1</b>	<b>7,7</b>	<b>11,9</b>	<b>4,8</b>





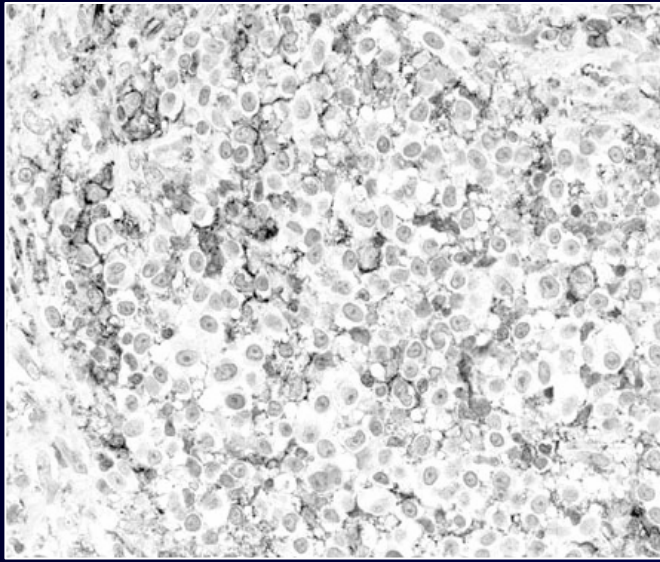
**CD31 / PECAM-1**  
**Platelet/Endothelial Cell Adhesion Molecule-1**

- **Glicoproteina Transmembrana, 130-kD**
- **Riconosciuta dal Mab JC/70A**
- **Espressa da:**
  - **Endotelio**
  - **Megacariociti**
  - **Piastrine**



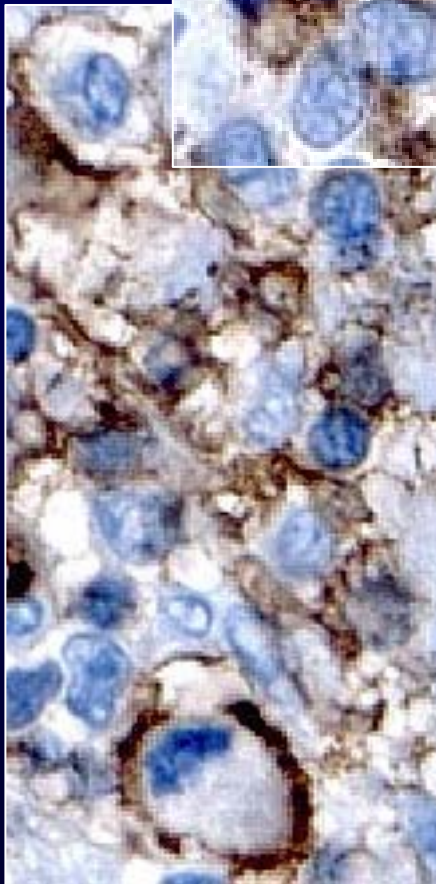
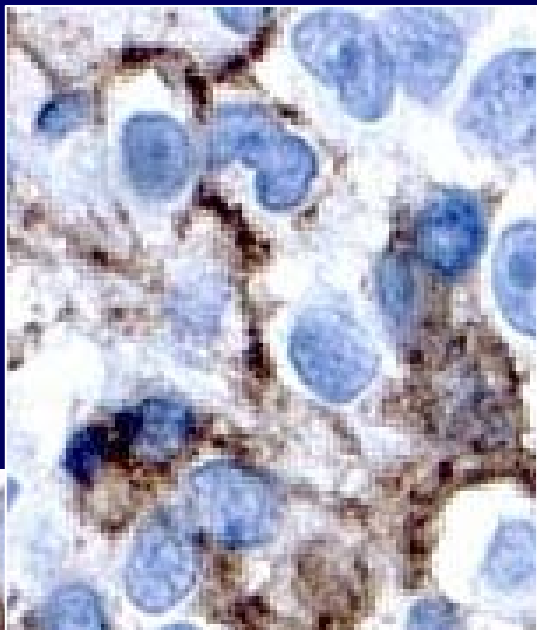
# IMITAZIONE VASCULOGENICA TUMORALE

## “Vasculogenic Mimicry”



**Rete canalicolare extracellulare delimitata da matrice extracellulare generata dalle cellule tumorali, che Simula un evento vasculogenico microcircolatorio**

- **Descritta in vivo in molti tumori maligni umani, in associazione con aggressività tumorale, stadi avanzati di progressione, prognosi sfavorevole**
- **Abbozzo di paracircolazione intratumorale per lo scambio fluido extravascolare (“*Fluid-Conducting Meshwork*”)**
- **Associata alla deregolazione di geni coinvolti nell’angiogenesi: CDH5, EPHA2, LAMC2**



**CD31  
Negativi**

**CD31 Positivi  
(+, ++, +++)**

<b>POLIPI FOBT</b>	<b>13 (40%)</b>	<b>20 (60%)</b>
<b>POLIPI ENDOSCOPIA</b>	<b>59 (65%)</b>	<b>31 (35%)</b>

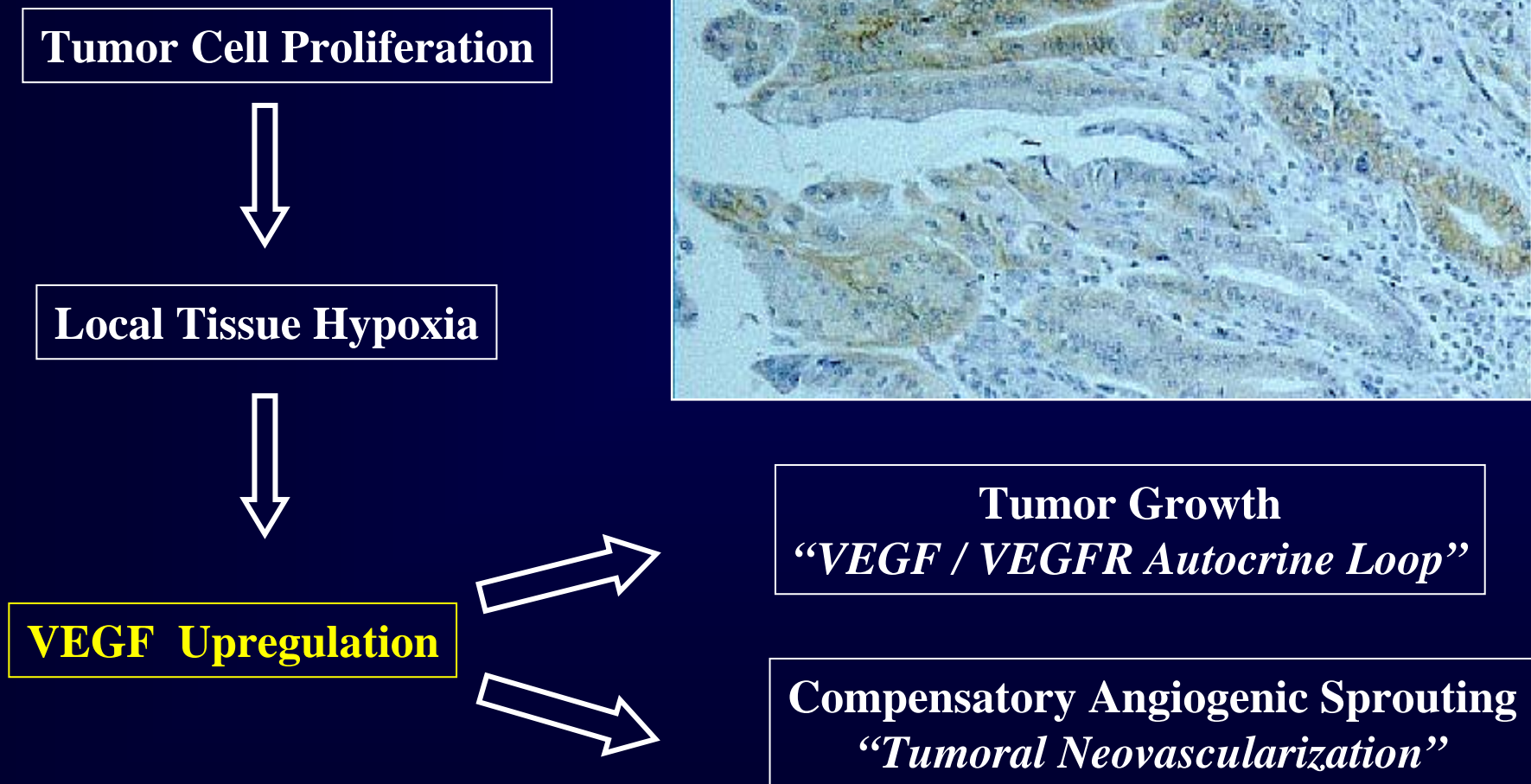
	<b>Negativi</b>	<b>Fase 1</b>	<b>Fase 2</b>	<b>Fase 3</b>
<b>CD31 -</b>	<b>61 / 81 (75%) *</b>	<b>2 / 18 (11%)</b>	<b>2 / 16 (13%)</b>	<b>0 / 8</b>
<b>CD31 +</b>	<b>7 / 81 (9%)</b>	<b>5 / 18 (28%)</b>	<b>5 / 16 (31%)</b>	<b>1 / 8 (12%)</b>
<b>CD31 ++</b>	<b>7 / 81 (9%)</b>	<b>5 / 18 (28%)</b>	<b>5 / 16 (31%)</b>	<b>4 / 8 (50%)</b>
<b>CD31 +++</b>	<b>6 / 91 (7%)</b>	<b>6 / 18 (33%)</b>	<b>4 / 16 (25%)</b>	<b>3 / 8 (38%)</b>

***p = 0.000 vs CD31 positivo (+, ++, +++)***



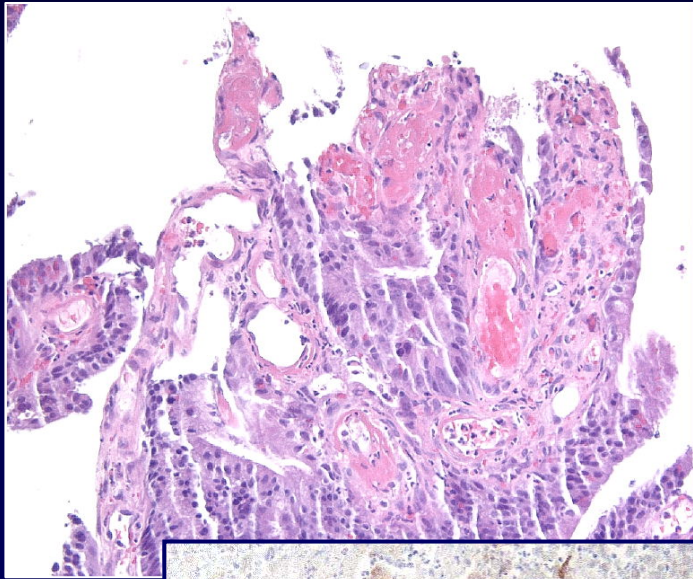
# Polipi FOBT+:

## Vascular Endothelial Growth Factor (VEGF)

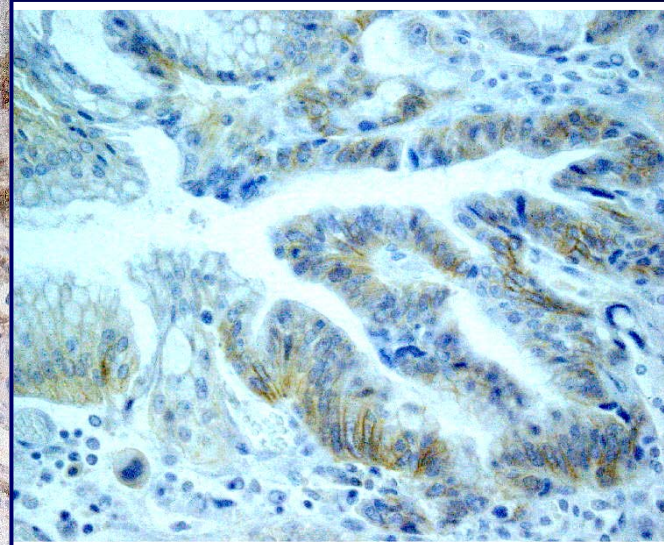
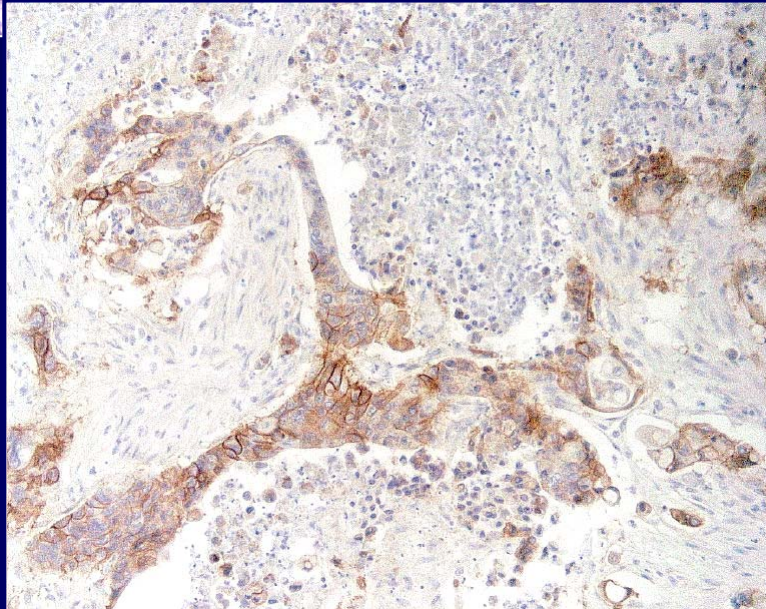


# Polipi FOBT+:

## Espressione Omeostatica di VEGF



- **Promozione Angiogenesi**
- **Aumento Permeabilità Vascolare**
- **Migrazione Cellule Endoteliali**
- **Proliferazione Endoteliale**
- **Rimodellamento Tissutale**



# **MOLECULAR PROFILING OF FOBT-DETECTED COLORECTAL POLYPS**

**Risio M, Senore C, Pera A, Segnan N.**

## **ACHIEVEMENTS:**

- ✓ **Morphogenetic Features Sustaining FOBT Detection of Polyps Have Been Identified**
- ✓ **Microvasculature Scaffold Is Unmodified in Bleeding Polyps**
- ✓ **Vasculogenic Mimicry (Vascular Transdifferentiation) is Frequently Occurring Among FOBT+ Polyps**
- ✓ **An Autocrine Loop VEGF-VEGFr Might Act After Bleeding as Repairing Mechanism**

## **GOALS:**

- ✓ **To Identify Genetic/Epigenetic Profiles Associated with Vasculogenic Mimicry**